PROCEEDINGS

OF THE

American Chemical Society

FOR THE YEAR 1919

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PROCEEDINGS.

Contents.

January.

General Society Minutes and Reports . 1
Council Minutes 1
Directors' Minutes 5
Council 7
Members elected between Nov 15 and December 15 1918 7
Meetings of the Sections
  Cleveland Section 11
    The Manufacture of Enamel Lined Apparatus E P Poste Refractory Materials as a Field for Research, E W Washburn
  Connecticut Valley Section 11
    Some Problems of Gas Warfare, E B Spear
  Detroit Section 12
    The Manufacture of Synthetic Phenol in the United States, L D Vorce The Industrial Uses of Oxygen S H Calender Electric Furnaces for the Laboratory, W D Little
  Eastern New York Section 12
    Projected Arc Images in a New Method of Chemical Analysis and Photo Chemical Uses of the Flaming Arc, W R Mott
  Georgia Section 12
    The Food Constituents and Their Utilization, A M Muckenfuss
  Indiana Section 12
    Solubility, E C H Davies
  Louisiana Section 12
    The Preparation of Active Decolorizing Carbons, II, F W Zerban
  Maryland Section 12
  Michigan Agricultural College Section 12
    Chemistry after the War, E W Rockwood
  Milwaukee Section 12
    Some Results of New Investigations of the Chemistry of the Keratins, L Kahlenberg Cooking Food Products without Loss of Flavor or Substance by Means of Low Temperature Combined with High Atmospheric Pressure, F S Hadley
  Minnesota Section 12
  Nashville Section 13
    The Potash Situation, E E Ransom Powder Manufacturing as a Chemical Industry, C W Chappell
  New Haven Section 13
    The Metallurgy and Heat Treatment of Ordnance Steel, C E McQuigg
  New York Section 13
    The Manufacture of and the Use of Toxic Gases, W H Walker The Manufacture of Gas Defense Apparatus, B Dewey
  Pittsburgh Section 13
    Chemical Considerations in Moulding Sand Practice in Europe and Amer

ica, P G H Boswell S A T C at the University of Pittsburgh, A Silverman
Rhode Island Section 13
Some Problems of Gas Warfare, E B Spear
Rochester Section 13
Gas Warfare, W D Bancroft
St. Louis Section 13
Electrolytic Zinc, O H Pierce Coal Tar Crudes and Coal Tar Derivatives, J Bebie Coal Tar Crudes and Intermediates J Bebie
Syracuse Section 14
Some Organic Compounds of Arsenic of Medicinal Value, R S Boehner
Washington Section 14
Preparation of Organic Chemical Reagents R Adams The Value of a Museum of Chemical Compounds, C L Alsberg
Western New York Section 14
The Great Bridge Spans of America F W Skinner The Chemist of the Future, E Hendrick
Wisconsin Section 14
Some Recent Experiments on the Acid Bessemer Converter, R S McCaffery The Status of Chlorine in Plant Nutrition W E Tottingham
Deceased Members 14

February.

Report of the Secretary of the American Chemical Society for the Year 1918 15
Report of the Editor of the Journal of the American Chemical Society for the Year 1918 18
Report of the Editor of Chemical Abstracts for the Year 1918 19
Report of the Editor of the Journal of Industrial and Engineering Chemistry for the Year 1918 21
Council 22
Members elected between December 15, 1918 and January 15 1919 24
Meetings of the Sections
Alabama Section 35
A Review of the Sources and Production of Nitrogen Compounds, J P Montgomery The Criteria in the Declaration of Chemical Independence in the United States I Newton Kugelmass
Chicago Section 35
Some Recent Chemical Researches on the Preparation of Food, Katherine Blunt
Cincinnati Section 35
On the Nature of Cohesion and Its Relation to Chemical Affinity, Alfred P Mathews
Cleveland Section 35
The Use of X Rays in Crystal Analysis, Ancel St John
Connecticut Valley Section 35
The Chemical Aspects of Modern Theories of Nutrition, H W Wiley
Delaware Section 35
Some Phases of Reconstruction in Belgium, A Knops Chemistry as She is Taught, A Smith
Detroit Section . 36
The Industrial Uses of Oxygen, S H Calender Electric Furnaces and Pyrometers, W A Gatward Pharmaceutical Chemistry, F O. Taylor

Shall Educational Institutions Continue their Former Policy of Importing Apparatus and Chemicals, Duty Free? J C Moore Coöperation between the University and the Manufacturing Industries, W L Badger

Indiana Section 36

Slag Enclosure in Steel and Iron, E G Mahin

Kansas City Section 36

Chemistry as Applied to the Flour Industry, C J Patterson

Lexington Section 37

The Oxidation of Sulfur in Soils as a Means of Increasing the Availability of Mineral Phosphates, O N Shedd Note on the Decomposition of Diluted Lime-Sulfur Solution, S D Averitt Gastric Digestion, O R Clutter Gas Warfare, P S Blumenthal and Wm Rodes

Maryland Section 37

Platinum, S J Lloyd The Study of the Chemistry of Blood and Urine, E U McCollum

Michigan Agricultural College Section 37

The Manufacture of Picric Acid in United States, H S Reed.

Nashville Section 37

Methods of Detecting Small Quantities of Gold, W H Hollinshead

Pittsburgh Section 37

Synthetic Phenol Resins, L V Redman

Philadelphia Section 37

Grinding Wheels, H A Plusch Airplane Dopes, W H Smith Export Trade and Chemicals, C L Chandler The Manufacture of Prussian Blue and Prussiates, S Felton Grove

Puget Sound Section 38

The Missing Elements with Atomic Numbers 43 and 75, J D Ross

Rhode Island Section 39

Recovery of Light Oil Products at the Providence Gas Company, W M Russell

Rochester Section 39

Glass Development under War Pressure, A L Day The Development of a Research Synthetic Indigo, V J Chambers

St Louis Section 39

City Milk Supply, C R Nicolls

Toledo Section 39

Chemistry and the War, H R Kreider

University of Illinois Section 39

The Carbonization of Coal, S W Parr and T E Layng

University of Missouri Section 39

Virginia Section 39

Oysters, H V Stewart Tanning and Dye Wood Industry, B A Gish. Gas Warfare, Captain Bolenbaugh

Wisconsin Section 40

The Chemical Side of the War, Mayor Victor Lenher

Deceased 40

March.

Council 41

Advisory Committee Meeting 41

Report of the Treasurer for the Year 1918 42

Members elected between January 15 and February 15, 1919 46

Meetings of the Sections:

Ames Section 54
Chemistry after the War and the Future Policy of the American Chemical Society (General Discussion). Poisonous Gases: Some Chemical Problems in their Manufacture, J. A. Wilkinson.
Chicago Section 54
Some Recent Researches on the Chemistry of the Keratins, L. Kahlenberg.
Cincinnati Section 54
The Use of Gas in Warfare, R. F. Bacon.
Cleveland Section 54
The American Chemist in the Recent War and His Part in the Future Development of This Country, Major General W. L. Sibert.
Connecticut Valley Section 54
The Refining of Copper, Stanislaus Skowronski.
Cornell Section 54
Gas Warfare, Captain H. S. Bennett.
Delaware Section 55
Refractory Materials as a Field for Research, E. W. Washburn.
Lexington Section 55
Research as a Factor in University Progress, F. L. McVey.
Louisiana Section 55
American Polariscope (Discussion). The Deterioration of Cane Sugar Caused by Fungi, N. Kopeloff and Lillian Kopeloff.
Maryland Section 55
The Manufacture and Use of Toxic Gases, Col W. H. Walker.
Milwaukee Section 55
A Symposium on the Milwaukee Water Supply.
New Haven Section 55
Laboratory and Table Glassware, S. R. Scholes.
Northern Intermountain Section 55
The Relationship of the Chemical and Bacteriological Analysis of Water, J. H. Jonte. Gas Warfare, G. McMahon, G. Kildow.
Philadelphia Section 56
The Camera and the War, C. E. K. Mees. Charter Revision, R. Duane. Lutes and Cements, S. Sadtler.
Pittsburgh Section 56
Tactical Uses of Gases in Warfare, Colonel R. F. Bacon.
Puget Sound Section 56
Research Work of the Chemical Warfare Service, H. G. Byers. Engineering Education, J. L. Hall.
Rhode Island Section 56
Rhode Island Minerals from the Standpoint of the Curator, H. L. Madison.
Rochester Section 56
Synthetic Cyanide and its Derivatives, Freeman. Fine Organic Chemicals, H. T. Clarke.
St. Louis Section 56
The Chemistry of the North American Indians, H. M. Wh.
Syracuse Section 56
Piezo Electricity, A. M. Nicolson.
Toledo Section 57
Activities of the Chemical Warfare Section, Col. F. M. Dorsey.

University of Illinois Section 57
Chemistry of Gas Offensive Warfare, R. Adams.
University of Michigan Section 57
The Early History of the Element, W. G. Smeaton.
University of Missouri Section 57
Operation of the Respiration Calorimeter, C. R. Moulton. Factors Effecting the Growth of Dairy Cattle, C. H. Eckles.
Washington Section 57
Airplane Dopes, W. H. Smith. The Preparation of Metol, R. N. Harger. The Removal of Phosphine from Ammonia Made from Cyanamide, J. D. Davis.
Western New York Section 57
Relation of the Patent Lawyer to the Chemist and Engineer, J. C. Pennie.
Deceased 57

April.

Minutes of the Advisory Committee Meeting 59
Members elected between February 15 and March 15, 1919 61

Meetings of the Sections

California Section: 66
Experiences in the Chemical Warfare Service with the American Expeditionary Forces in France, Lt. Col. J. H. Hildebrand. Metallic Salts of Tyrol, Indol, and Carbazol, E. C. Franklin. Manufacture of Gas Defense Chemicals, Capt. W. E. Brophy.
Cleveland Section 66
Industrial Utilization of Chemical Research, Arthur D. Little.
Detroit Section 66
Shall Educational Institutions Continue the Plan of Importing Chemicals and Apparatus, Duty Free? J. C. Moore. Aids in Laboratory Technique, H. Spurrier.
Indiana Section 66
Creosote Oils, Their Grading, Use and Production, T. W. Smith. An Epizootic Apparently Due to the Assumption of High Pathogenicity by an Organism Usually a Non-Pathogen, E. A. Cahill. Mustard Gas and Other War Gases, G. H. A. Clowes.
Maryland Section 66
Gas Defense, A. B. Lamb.
Michigan Agricultural College 66
Experiences at the American University, Washington, D. C., during the War, E. J. Miller. Symposium on Phosphorus, A. J. Patten.
Milwaukee Section 67
Gas and Flame as Modern Weapons of Warfare, Major J. H. Mathews.
Nashville Section 67
Atmospheric Carbon Dioxide and Its Relation to Human Life, H. A. Webb.
New Haven Section 67
The Future of Industrial Organic Chemistry, H. Hibbert.
New York Section 67
The True Story of Camouflage, M. Toch. Aerial Photography, N. Bronson.
Pittsburgh Section 67
The Selection, Production and Development of Aircraft Material, Major G. L. Norris.

Puget Sound Section.......... 67
The Metallography of Electric Welding, A. G. Bissell. A Survey of Chemical Manufacturing Possibilities, H. K. Benson.
Rhode Island Section.......... 67
The Development of the Gas Filled Lamp, W. E. Smith.
Rochester Section.......... 67
Cellulose, H. LeB. Gray.
St. Louis Section.......... 67
Some Chemical Problems of the Feeding Stuff Industry, G. P. Plaisance.
Syracuse Section.......... 68
Piezo Electricity, A. McL. Nicolson.
Toledo Section.......... 68
Colloids, H. N. Holmes.
University of Illinois Section.......... 68
Valence, W. A. Noyes.
University of Michigan Section.......... 68
Notes on Some Modern Explosives, M. Gomberg.
Vermont Section.......... 68
Gas Warfare, C. R. Hoover.
Virginia Section.......... 68
Poisons and Poisonings, J. M. Whitfield.
Washington Section.......... 68
Present Status of the Nitrate Industry in the United States, A. H. White. The National Research Council, J. Johnston. Chemical Protection against Poisonous Gases, A. B. Lamb.
Deceased.......... 68

May.

Minutes of the General Meeting, Buffalo, N. Y.......... 83
Minutes of the Directors' Meeting.......... 84
Council Minutes.......... 85
Members elected between March 15 and April 15, 1919.......... 103
Meetings of the Sections:
Ames Section.......... 108
Pyrometry, Especially as Applied to Industrial Measurements of High Temperatures, O. L. Kowalke.
California Section.......... 108
Some Chemical and Medical Properties of the Saccharomyces Cerevisiae (Yeast), H. Arnstein.
Chicago Section.......... 108
Dietetics of Butter and Oleomargarine, W. D. Richardson. Explosives, W. V. Evans. Food and Nutrition Survey, C. K. Beebe. Gas Production, L. Hellerman. Gas Service in the Field, E. D. Gothwaite. Experiences and Experiments, C. H. Milligan. Research in the C. W. S, G. L. Wendt.
Cleveland Section.......... 109
Activities of the Offensive Division, Chemical Warfare Service, Wm. McPherson.
Columbus Section.......... 109
The Inter-Allied Gas Warfare Conference, Wm. McPherson. Interesting Engineering Features of Gas Warfare Production, D. J. Demorest.

Connecticut Valley Section 109
The Relation of Fertilizers to Food Production in the United States, E. J. Pranke. Wheat Flour and Its Toxic Action on Yeasts, Chas. A. Glabau.
Delaware Section 109
Camphor Cultivation in the United States, F. A. Gudger. Colloid Chemistry, W. D. Bancroft.
Detroit Section 109
Detroit's Need of a Filtering Plant, J. E. Clarke. Pharmaceutical Solvents, W. Scoville.
Eastern New York Section 109
A New Theory of Atomic Structure, Irving Langmuir.
Georgia Section 109
Chemical Warfare Service, C. L. Parsons. A Compendia of American Chemical Literature, A. Seidell.
Indiana Section 109
Nux Vomica and its Alkaloids, I. L. Miller. Sausages, H. E. Bishop. The Function of a Laboratory in Water Purification, L. R. Taylor.
Kansas City Section 110
Applications of Electrometric Methods of Determining Acidity in Soils, Flour, and Amino Acids, E. L. Tague.
Lehigh Valley Section 110
Chemical Literature, Harvey F. Mack. Production of Pure Chemicals, George P. Adamson. Cement Production, Louis Anderson. Analytical Chemistry, Porter W. Shimer. Education of Chemists, Edward Hart.
Louisiana Section 110
A Critical Study of the Development of the Sugar Industry, L. A. Becnel. How the Chemist Can Best Help the Community, W. L. Howell, C. F. Williamson, Jr., F. W. Liepsner.
Michigan Agricultural College Section 110
The Measurement of Hydrogen ion Concentration, and Some of its Chemical and Biological Applications, C. S. Robinson.
Milwaukee Section 110
Applied Meteorology, A. A. Justice.
Minnesota Section 110
Research in Offense; Problems in Gas Warfare, Lauder W. Jones.
Nashville Section 110
The Desiccation of Vegetables, H. L. Walter. Some Substances which Interfere with Color Tests, E. A. Ruddiman.
Philadelphia Section 110
Chemicals from Kelp, C. E. Vanderkleed. The Recovery of Collodion Solvents in the Manufacture of Welsbach Mantles, C. A Dodge. How the Chemist Can Use the Commercial Museum, W. P. Wilson. Philadelphia as a Commercial Center, E. J. Cattell. A Glimpse of Some Textile Processes, Elmer C. Bertolet.
Pittsburgh Section 111
Gas Flame and Smoke in this War, and the Next, W. H. Walker. The Relation between Chemical Structure and Physiological Action, Jacob Rosenbloom.
Puget Sound Section 111
Sympathetic Inks, Fred. C. Heath. Manufacture of Toxic War Gases, T. G. Thompson.

Rhode Island Section ... 111
  Chemical Warfare, W. K. Lewis.
Rochester Section ... 111
  Utilization of Kelp, C. A. Higgins. The Test Due at Work with the Yard Stick, H. E. Howe. Experiences in Service, Harry A. Carpenter, W. G. O. Christiansen, Otto Cook, Ivar Hultman, Garson Meyer, Thomas Murray, Lewis G. Smith, Leon S. Ward, Roland T. Will, Gerald Young.
St. Louis Section ... 111
  The Chemistry of Mesothorium, Herman Schlundt.
Syracuse Section ... 111
  Fine Organic Chemicals, H. T. Clarke.
Toledo Section ... 111
  A Study of the Mechanism of Certain Reactions of Hydroxylamin, A. MacKenzie. Testing Dry Cells, Ida F. Starkweather. Railway Signalling, R. W. Erwin.
University of Illinois Section ... 111
  Heterogeneous Equilibria between Aqueous and Metallic Solutions, G. McP. Smith. Some Phases in the Development of the Paint Industry, E. C. Holton.
University of Michigan Section ... 112
  Aerial Photography in War Time and Peace, Theodore Williams.
University of Missouri Section ... 112
  Manufacture of Smokeless Powder, Mary V. Dover.
Virginia Section ... 112
  The Perfection of a Paper Product to Filter Toxic and Irritating Smokes Out of the Air, H. W. Ellerson. Some of the Problems Connected with the Platinum Group of Metals, J. L. Howe.
Washington Section ... 112
  Optical Glass, A. L. Day.
Wisconsin Section ... 112
  The Use of Metal as Catalysts in Hydrogenation—The Role of the Metal, L. Kahlenberg. The Organic Aspect of Reduction, E. Kremers. Reduction of Azulene, R. E. Kremers. Hydrogenation of Cottonseed Oil, G. Ritter. The Reduction of Dihydroxythymoquinone, Nellie Wakeman.
Deceased ... 112

June.

Council ... 113
Members elected between April 15 and May 15, 1919 ... 113

Meetings of the Sections:

  Alabama Section ... 116
  Agricultural Experiment Station and Extension Work in Alabama, J. F. Duggar. Soil Acidity in its Relation to Plant Growth, M. J. Funchess.
Ames Section ... 116
  Some Interrelations of Biochemistry and Bacteriology, R. E. Buchanan.
California Section ... 116
  Making Potash at Searles Lake, A. W. Morse.
Chicago Section ... 116
  The Chemistry of the Nerve Impulses, A. P. Mathews.
Cincinnati Section ... 116
  On the Penetration of "Mustard Gas" and Other War Gases into Living Tissue and the Mechanism of their Destructive Action, G. H. A. Clowes.

Columbia Section 116
Emulsions, Harry N. Holmes.
Connecticut Valley Section 116
Rubber, Theodore Whittlesey.
Cornell Section 117
Cellulose, H. LeB. Gray. The Primer Inspection Laboratory of the Ordnance Department and its Work, E. M. Chamot.
Delaware Section 117
The Work and Future of the University Union in Europe, H. B. Thompson. Flotation—Wolf Hall, Wm. G. Grosvenor.
Indiana Section 117
The Chemistry of Electrical Discharge through Gases, F. O. Anderegg.
Iowa Section 117
Atomic Surfaces and Molecular Attraction, W. D. Harkins. Chemical Examination of Some Dolomites, Nicholas Knight. The Manufacture of Ammonium Nitrate for Explosives, J. A. Bahm. Steric Effects in the Acylation of Amino Phenols, L. Chas. Raiford.
Kansas City Section 117
Hydrocarbons, Gustav Egloff Chemical Warfare Service Laboratories in Paris, G. W. Stratton.
Lehigh Valley Section 117
Potash Recovery, R. K. Meade.
Lexington Section 117
Gas Warfare, A. S. Loevenhart. The Twitchell Process in the Saponification of Fats, A. O. Snoddy.
Louisiana Section 118
A Discussion and Criticism of Current Analytical Methods; Old and New Uses of Industrial Alcohol, F. W. Leipsner.
Maryland Section 118
Colloids, W. D. Bancroft. The Moisture Content of Coal, with Some General Remarks on the Genesis of Coal, G. A. Hulett. Some Commercial Aspects of the Haber Process, Taylor.
Milwaukee Section 118
Some Experiences of a Gas Officer in the First Army, A. E. F., J. H. Walton. A Talk on Oils, P. H. Peters. Insecticides, C. B. Dickey.
Minnesota Section 118
Contribution of Radium to Chemistry and Medicine, G. L. Wendt.
Nashville Section 118
The Paragenesis of Some Tennessee Minerals, W. A. Nelson.
New Haven Section 118
Some Bearings of Physical Chemistry on Technical Problems, John Johnston.
New York Section 118
American Scientific Glass—The Reward of Research, H. E. Howe.
Philadelphia Section 118
Planning a Factory, E. L. Knoedler. Chemistry and Commerce, C. O. Althouse.
Pittsburgh Section 119
Recent Investigations in the Chemistry of Nutrition, E. V. McCollum.
Puget Sound Section 119
Methods for Determination of Manganese, T. Dunlap. What Industry

Expects of the Student, H K Benson Addition *vs* Dissociation, W. L. Gilliland.
Rhode Island Section . .. 119
Synthetic Rubber, R B Earle
Rochester Section 119
Some Practical Applications of the Hydrogen Ion Concentration of Milk, L. L. Van Slyke Coöperative Research Laboratories, C E Kenneth Mees
St. Louis Section 119
Some Recent Studies Connected with the Coking of Coal, S W Parr
Southern California Section 119
Leaves from a Chemist's Note Book on the Work of the Agricultural Experiment Stations, S R Mitchell
University of Missouri Section 119
Control and Function of Pigments in Fowls L S Palmer
Vermont Section 119
Chemical Microscopy, E M Chamot
Virginia Section 119
Recent Advances in Physics R F Loving
Wisconsin Section 120
Adjusting the American Army to the Conditions of Gas Warfare, J H Walton
Deceased 120

July.

Council 121
Members elected between May 15 and June 15, 1919 121
Meetings of the Sections
Chicago Section 123
The Chemical Exposition, C F Roth
Cleveland Section 123
Chemistry and Human Efficiency, C H Herty
Connecticut Valley Section 123
Cornell Section 124
Optical Glass for War Purposes, A L Day The Dennis Barett War Plant for Synthetic Phenol, F B Johnson
Detroit Section 124
Lexington Section 124
The Use of the Microscope in Analytical Chemistry E M Chamot
Minnesota Section 124
Organic Mercurials, F C Whitmore
Nashville Section 124
New Haven Section 124
War Gases, F P Underhill
New York Section 124
Studies in Chemotherapy (A) The Synthesis of New Types of Arsenic Compounds, W A Jacobs and M Heidelberger, (B) Biological Studies on the New Types of Arsenic Compounds, W H Brown and L Pearce Technology of Organic Arsenicals—Particularly Arsphenamine, A E Sherndal Synthetic Studies on the Cinchona Alkaloids, M Heidelberger and W. A Jacobs Developments in the Production of Cinchona Alkaloids, H Schaeffer

- **North Carolina Section** 124
  - Some Recent Developments in the Manufacture of Metallic Tantalum and Columbium, E S Ross New Naphthalene Dyes, A S Wheeler. Investigations on the Nitrotoluenes, J M Bell A New Seed Oil from the Cockle-burr, L B Rhodes Certain Compounds of Zirconium and Oxyhalogen Acids, F P Venable and I W Smithy The Reaction between Hydrochloric Acid and Potassium Permanganate, F P Venable and D H. Jackson
- Northern Intermountain Section 125
  - Ferro-Tungsten, C G Warfel Instantaneous Reactions in Non-Aqueous Solutions, C J Baldwin
- St Louis Section 125
  - The Work of the Edgewood Arsenal, G F Siemers Chemical Warfare Service with the American Expeditionary Forces, M E Webber
- Southeast Texas Section 125
  - Synthetic Ammonium Nitrate Manufacture at Sheffield, Alabama, S P Puddicomb Color Photography, F Hall The Activities of the American University Station during the War E Streeter Properties and Treatment of Oil-Field Emulsions (Goose Creek Emulsions), J L Shrttivk
- Syracuse Section 125
  - The Arrangement of Electrons in the Atom and the Molecule, I Langmuir
- University of Illinois Section 125
  - The Quinhydrone Hypothesis of Plant Pigmentation, E Kremers
- University of Michigan Section 125
  - The Problems and the Equipment of the Evaporator Laboratory, W L Badger
- Washington Section 125
  - The Work of the Color Laboratory of the Bureau of Chemistry, H D Gibbs The Commercial Preparation and Some of the Commercial Applications of the Enzymes Invertase, K P Munroe

Deceased 126

August.

Council 127

Members elected between June 15 and July 15, 1919 127

Meetings of the Sections

- Toledo Section 128
  - Railway Signalling, R W Erwin

Van't Hoff Fund. 128

Deceased 129

September.

Council 131

Members elected between July 15 and August 15 1919 131

Meetings of the Sections

- California Section 132
  - Positive and Negative Valence, W A Noyes Chemistry and Naval Warfare, J Kendall

Deceased Members 132

October.

Minutes of Directors' Meeting 133

Minutes of the General Meeting, Philadelphia, Pa , Sept 2-6, 1919 134

Minutes of Council Meeting 138
Members elected between August 15 and September 15, 1919 144
Deceased Members 146

November.

Council 147
Members elected between September 15 and October 15, 1919 147
Report of Committee on the Late Lord Rayleigh 149

Meetings of the Sections:

- Alabama Section 151
  - Some Volatile Oils from Native Alabama Plants, E. R. Miller. Chemistry in the Foundry, J. T. MacKenzie
- California Section 151
  - Research behind the Battle Line, J. H. Hildebrand.
- Cincinnati Section 151
  - Chemical Change during the Passage of Nerve Impulse, S. Tashiro.
- Connecticut Valley Section 151
  - Some Phases of Gas Defence Work, F. P. Underhill.
- Lexington Section 151
  - An Account of the Philadelphia Meeting, F. E Tuttle. The Cause of Deterioration and Spoiling of Corn and Corn Meal, J. S. McHargue. The Effect of Calcium on the Composition of the Eggs and Carcass of the Laying Hen, G. D. Buckner.
- Louisville Section 152
- New York Section 152
  - The Future of Industrial Alcohols, B. R. Tunison. Ethyl Alcohol from Wood Waste, F. W. Kressmann. Higher Alcohols, G. F. Richmond. Alcohol from Sulfite Waste Liquor, R H. McKee. Use of Alcohol in the Dye Industry, L. H. Cretcher.
- Pittsburgh Section 152
  - Chemical War Industries Board; Conditions Abroad, C. H. McDowell. Problems Relating to the Chemistry of Coal, R. Thiessen.
- Rochester Section 152
  - The Chemistry of Nitrogen, A W. Browne
- Southeast Texas Section 152
  - Chemistry of the Packing Plant, L. S. Bushnell.

Deceased Members 152

December.

Council 153
Members elected between October 15 and November 15, 1919 153

Meetings of the Sections:

- Cincinnati Section 156
  - The Rare Earths, Their Production and Utilization, H. S. Miner.
- Cleveland Section 156
  - Some Principles Underlying Municipal Gas and Fuel Supply, R. S. McBride.
- Cornell Section 157
  - Gas Warfare, L. A. Maynard.
- Delaware Section 157
  - The Rubber Industry, W. C. Geer.
- Detroit Section 157
  - The Cause of the Sweet Taste of Organic Compounds, J. H. Ransom.

Indiana Section 157
Some Experiments with Free Fluorine, Frank C Mathers The Water Purification Plants of the Army Cantonments in the United States, Major H E Jordan The Water Purification Plants of France, Captain J C Diggs
Lehigh Valley Section 157
Some Innovations in Bethlehem-Built Apparatus, J G Lehman Chemical Engineering in the Bethlehem Steel Company, E R Shimer Metallurgy—Educationally and Technically, J W Richards Chemistry at Lehigh University, H W Ullmann Fuel Products, D S Chamberlain Linseed Oil in the Patent Leather Industry, J S Long
Lexington Section 158
The Rare Earths, Their Production and Utilization, Harlan S Miner
Maryland Section 158
Milwaukee Section 158
Imbibition, J A Wilson
Minnesota Section 158
Aristol, G H Woollett Some Experiences during the Crisis of 1914–15 in the American Dye Industry, L J Matos
Nashville Section 158
Drug Standardization, O V R Smith
New York Section 158
The Future of Industrial Alcohols B R Tunison Ethyl Alcohol from Wood Waste, F W Kressman Alcohol from Sulphite Waste Liquor, R H McKee Use of Alcohol in the Dye Industry, L H Cretcher Higher Alcohols, G F Richmond Cellulose Present Day Problems, W P Cohoe Cellulose Hydration Problems, J E Minor, read by Dr Wm H Gesell Nitrocellulose from Wood Pulp, H Bradshaw R G Woodbridge, Jr
Philadelphia Section 159
Bubbles, Lt Col W D Bancroft
Puget Sound Section 159
The Work of the Chemist in the Condensed Milk Industry with Special Reference to Recent Development in Laboratory Methods, P A Cornelius
Rochester Section 159
The Milk Problem in Rochester and Elsewhere, C E North Microstructure of Plain Carbon Steels and Some Defects Usually Encountered, W B Miller
St Louis Section 160
Baking Powder Chemicals, J T Meckstroth How Have the U S Chemical Manufacturers Met the Dyestuff Situation? F S Bacon The Synthesis of Carbohydrates in the Plant, F W Muncie
Syracuse Section 160
The Chemical Welfare Service Training Division, Major R A Baker
Toledo Section 160
The Fixation of Nitrogen, Colonel Alfred H White
University of Illinois Section 160
Structure of the Atoms and Its Bearing on Chemical Valence, I Langmuir
University of Michigan 160
The Fixation of Nitrogen, A H White.

University of Missouri Section 161
Effects and Treatment of Gas Poisoning, H. D. Hooker, Jr.
Virginia Section 161
Some Phases of the Problems of Fixation of Nitrogen, Graham Edgar.
Washington Section 161
Vanillyl Acid Amides, E K. Nelson. Growth Experiments with the Proteins of the Navy Bean, C. O. Johns and A. J Finks. A New Hexabromide Method for Linseed Oil, L. L Steele and F M. Washburn. Manufacture of Commercial Casein, W. M Clark and H F. Zoller Status and Prospects of the Dye Industry in the United States, C L Reese. Crystallography in the Service of the Chemist, E T. Wherry A Few Methods for the Study of Fumaroles, E T. Allen
Western New York Section 161
Patent Laws with Special Reference to the Work of the Peace Commission, J E. Pennie
Wisconsin Section 162
The Essential Problems in the Successful Application of Powdered Coal, W G Wilcox The Biological and Medical Aspects of the Chemical Warfare Service, A S Loevenhart.
Deceased Members 162

Issued with the December Number, 1919.

Proceedings.

COUNCIL.

Mr. H. E. Howe has been appointed a member of the Committee on Reagents and Apparatus.

MEMBERS ELECTED BETWEEN OCTOBER 15 AND NOVEMBER 15, 1919.

Adriano, Felipe T., Hartley Hall, Columbia University, New York City.
Albrecht, Herbert O., 8 Wendell St., Cambridge, Mass.
Allbright, W. B., 4937 Dorchester Ave., Chicago, Ill.
Bailey, E. M., Agricultural Experiment Station, New Haven, Conn.
Barns, Helen V., Flatwoods, W. Va.
Bartlett, Ethel L., 536 S. Liberty St., Winston-Salem, N. Carolina.
Bartow, Virginia, Goucher College, Baltimore, Md.
Beard, Leslie C., Jr., 1120 Linden Ave., Baltimore, Md.
Becker, Carl, Illini Hall, Wright St., Champaign, Ill.
Beebe, S. P., 417 Park Ave., New York City.
Bennett, Joseph, Windsor Print Works, North Adams, Mass.
Berger, Henry G., 407 W. Healey St., Champaign, Ill.
Berkeley, Cyril J., The Biological Station, Nanaimo, B. C.
Blew, Michael J., 101 W. Chestnut St., Louisville, Ky.
Bloomberg, John, cr. Freeport Sulphur Co., Freeport, Texas.
Bracken, Oliver L., 28 East 7th St., Chillicothe, Ohio.
Brenton, Walter, 1048 W. Market St., Akron, Ohio.
Brockman, Charles J., 3 N. Main St., Nazareth, Pa.
Brown, Ralph W., cr. American Bauxite Co., Bauxite, Ark.
Bryan, Russell R., Eureka, San Juan County, Colorado.
Buffington, R. M., 1614 Kentucky St., Lawrence, Kansas.
Bulbrook, Harry M., Indian Head, Md.
Busch, Henry P., 1006 Spruce St., Phila., Pa.
Byers, M. L., 16 Webster Place, E. Orange, N. J.
Cadwell, Sidney M., 561 W 58th St., New York City.
Cantwell, Garrett R., Elsmere, Delaware.
Carlson, Lewis H., cr. Frederick Stearns & Co., Detroit, Mich.
Casey, Richard G., 125 William St., Melbourne, Australia.
Chamberlain, Frederick H., 806 First Place, Plainfield, N. J.
Chen, T. Y., Box 105, Washington, Pa.
Church, John F., 121 Main St., Peabody, Mass.
Cole, J. Bishop, 807 Southern Ave., Mt. Washington, Pittsburgh, Pa.
Coven, Allen W., 1122 West Ave., Elyria, Ohio.
Creelman, Fred N., No. 49 Parker Hall, Bates College, Lewiston, Maine.
Davidson, Arthur W., 601 West 137th St., New York City.
Davidson, Harry, 6011 Osage Ave., Phila., Pa.
Davis, George W., Eagleville, Missouri.
Dick, Abraham H., 952 Tiffany St., New York City.
Duhring, Edwin L., cr. Charles Enen Johnson & Co., Phila., Pa.
Dunning, Joseph W., 18 Maple Terrace, Rahway, N. J.
Eaton, Carl H., 67 Murdock St., Youngstown, Ohio.
Eckels, H. L., 1922 Arch St., Phila., Pa.
Egidius, Thorvald F., Servaas Bolwerk 10, Utrecht, Holland.

Selders, Raymond E., 124 West 8th St., Oklahoma City, Okla.
Sellman, Frank R., 1344 48th Ave., San Francisco, Calif.
Sivitz, William I., Aluminum Co. of America, New Kensington, Pa.
Smith, K. Dolbeer, Syracuse Rubber Co., Syracuse, N. Y.
Smith, Leland R., 9908 Lamont Ave., Cleveland, Ohio.
Soars, C. Austin, 5003 Chester Ave., Phila., Pa.
Sporkin, Charles H., 1308 N. Seventh St., Phila., Pa.
Stewart, Andrew, 1442 Clifton St., N. W., Washington, D. C.
Svanoe, Hans, cr. Mrs. Taylor, 710 4th St., Niagara Falls, N. Y.
Swayze, Myron A., Texas Portland Cement Company, Houston, Texas.
Swett, Francis S., Fort McKinley, Portland, Maine.
Tabern, G. W., 10 Twelfth St., Detroit, Mich.
Taft, Robert, Ottawa University, Ottawa, Kansas.
Thomas Theodore, 717 Forbes St., Pittsburgh, Pa.
Trevithick, Gladys I., 424 Duck St., Stillwater, Okla.
Updike, Ira A., The Graduate College, Princeton Univ., Princeton, N. J.
Vandaveer, F. Ewart, 604½ E. Stoughton St., Champaign, Ill.
Van Tassel, Edward D., Jr., 120 Franklin St., Newton, Mass.
Vaupel, H. F., cr. El Reno Mill & Elv. Co., El Reno, Okla.
Wade, W. M., 385 Pilgrim Ave., Highland Park, Detroit, Mich.
Wakefield, R. A., Va. Union University, Richmond, Va.
Wallis, Charles H., 703 Wynnewood Road, Phila., Pa.
Walter, Albert, cr. Stauffer Chemical Co., Inc., Chauncey, N. Y.
Watson, Ralph A., 333 So. 12th St., Phila., Pa.
Webber, Wolfert G., Harvard Mecidal School, 240 Longwood Ave., Boston, Mass.
Welcome, Carl J., Wallaceburg, Ontario, Canada.
Wendkos, Jesse, 1252 S. 17th St., Phila., Pa.
Wood, Howard D., 174 Holland St., Lewiston, Maine.
Wood, Robert E., 918 Court Merill, Mitchell, So. Dakota.
Zilliok, William G., 603 Vernon Ave., W., Fergus Falls, Minn.

CORPORATION MEMBER.

Carnotite Reduction Co., 2553 South Park Ave., Chicago, Ill.

MEETINGS OF THE SECTIONS.

[Full accounts of all meetings should be sent to Secretary Charles L. Parsons, 1709 G Street, N. W., Washington, D. C]

CINCINNATI SECTION.

The regular meeting of the Cincinnati Section was held Wednesday evening, November 12.

Program: "The Rare Earths, Their Production and Utilization," with special reference to Thorium, Cerium and Mesothorium; illustrated by lantern slides, samples, etc., by Dr. H. S. Miner. A. O SNODDY, *Secretary.*

CLEVELAND MEETING.

The first Autumn meeting of the Cleveland Section of the American Chemical Society was held Monday, November 3.

Mr. R. S. McBride, Engineer Chemist, of the U. S. Bureau of Standards, discussed, "Some Principles Underlying Municipal Gas and Fuel Supply."

R. D. LANDRUM, *Secretary.*

COLUMBUS SECTION.

Met on Friday evening, October 31. Dr. Harvey W. Wiley addressed the Section and was the guest of the Section at an informal dinner.

Jesse E. Day, *Secretary*.

CORNELL SECTION.

The Section met at Morse Hall, Thursday, October 30, 1919. Program: "Gas Warfare," by Dr. L. A. Maynard.

F. R. Georgia, *Secretary*.

DELAWARE SECTION.

Regular meeting, Wednesday, October 29, 1919, Wilmington, Del. Address: "The Rubber Industry," by Dr. W. C. Geer, Vice-President of the B. F. Goodrich Company.

J. Howard Graham, *Secretary*.

DETROIT SECTION.

The one hundredth and tenth meeting of the Detroit Section was held Thursday evening, October 16. The speaker of the evening was Dr. J. H. Ransom, of the Michigan Smelting Co., on the topic: "The Cause of the Sweet Taste of Organic Compounds."

D. S. Perry, *Secretary*.

INDIANA SECTION.

The October meeting of the Indiana Section of the American Chemical Society was held Friday, October 17. Speaker: Dr. Frank C. Mathers, Assistant Professor of Chemistry, Indiana University. Subject: "Some Experiments with Free Fluorine."

The following officers were elected: *President*, H. W. Rhodehamel; *Vice-President*, E. G. Mahin; *Secretary and Treasurer*, E. B. Carter, 2615 Ashland Ave., Indianapolis; *Executive Committee*, Helen C. Gillette, J. C. Diggs, and R. Chester Roberts.

The Indiana Section of the American Chemical Society met Friday, November 14, 8.00 P.M. Speakers: Major Harry E. Jordan, Supt. of Filtration, Indianapolis Water Co. Subject: "The Water Purification Plants of the Army Cantonments in the United States;" and Captain John C. Diggs, Water Engineer State Board of Health. Subject: "The Water Purification Plants of France."

Edgar B. Carter, *Secretary*.

LEHIGH VALLEY SECTION.

The Lehigh Valley Section met at Lehigh University on November 14.

Program: Mr. J. George Lehman, General Manager of the Bethlehem Foundry and Machine Company, "Some Innovations in Bethlehem-Built Apparatus." Mr. E. R. Shimer, Sales Metallurgist, Bethlehem Steel Company, "Chemical Engineering in the Bethlehem Steel Company." Professor J. W. Richards, "Metallurgy—Educationally and Technically." Professor H. W. Ullmann, "Chemistry at Lehigh University." Professor D. S. Chamberlain, "Fuel Products." Professor J. S. Long, "Linseed Oil in the Patent Leather Industry."

LEXINGTON SECTION.

The 57th meeting of the Lexington Section of the American Chemical Society was held on Thursday, November 13, 1919.

Program: An illustrated lecture by Mr. Harlan S. Miner, Chief Chemist of the Welsbach Company of America, Gloucester City, New Jersey. Subject: "The Rare Earths, Their Production and Utilization," with special reference to Thorium, Cerium, and Mesothorium.

GEO R. BANCROFT, *Secretary.*

MARYLAND SECTION.

The 37th regular meeting of the Maryland Section of the American Chemical Society was held on Friday evening, October 17, at which officers for the ensuing year were elected as follows: Dr. Frederick C. Blanck, *Chairman;* Mr. F. M. Boyles, *Vice-Chairman;* Mr. C. Clifton Howes, *Secretary.*

C. CLIFTON HOWES, *Secretary*

MILWAUKEE SECTION.

October meeting, Friday, October 24.

Mr. John A. Wilson, Chief Chemist of A. F. Gallun & Sons Co., gave a paper on, "Imbibition."

MINNESOTA SECTION.

October meeting, Friday, October 17.

Program: "Aristol," by Dr. G. H. Woollett.

At the meeting of the Minnesota Section, held October 23, the following officers were elected: *Chairman,* Lauder W. Jones; *Vice-Chairman,* R. A. Gortner; *Secretary,* Frank C. Whitmore; *Treasurer,* C. J. V. Pettibone; *Councilors,* E. P. Harding and W. H. Hunter.

Program: Dr. Louis J. Matós spoke on "Some Experiences during the Crisis of 1914–15 in the American Dye Industry."

FRANK C WHITMORE, *Secretary.*

NASHVILLE SECTION.

The 62nd meeting of the Section was held on Friday evening, November 7.

Program: An illustrated lecture on "Drug Standardization," by Mr. O. V. R. Smith, of Parke Davis & Co.,

H. A. WEBB, *Secretary.*

NEW YORK SECTION.

The New York Section met at Rumford Hall on June 6. The meeting was preceded by a dinner at the Chemists' Club. After a short business meeting the following papers were delivered:

"The Future of Industrial Alcohols," B. R. Tunison. "Ethyl Alcohol from Wood Waste," F. W. Kressman. "Alcohol from Sulfite Waste Liquor," Ralph H. McKee. "Use of Alcohol in the Dye Industry," Leonard H. Cretcher. "Higher Alcohols," G. F. Richmond.

The Section met on November 7 at the Chemists' Club. The following resolutions on the death of T. J. Parker were read and adopted by a rising vote:

Whereas, At the regular monthly meeting of the New York Section of the American Chemical Society, held on November 7, 1919, the announcement of the demise, on October 9, of Thomas J. Parker, our loyal companion and beloved friend, was received with profound sorrow; be it therefore

Resolved, That in Thomas J. Parker the New York Section has lost one of its oldest and most valued members, whose unceasing efforts and services in its behalf have materially contributed to the growth and prosperity of the Section.

Resolved, That the Section convey its expression of sorrow and sympathy to the bereaved family; and further be it

Resolved, That a copy of this resolution be spread upon the records of the Section, and that a copy thereof be transmitted to the family of Thomas J. Parker.

The following papers, on the general subject of "Cellulose Problems" were delivered:

"Cellulose: Present Day Problems," Wallace P. Cohoe. "Cellulose Hydration Problems," J. E. Minor; read by Dr. Wm. H. Gesell "Nitrocellulose from Wood Pulp," Hamilton Bradshaw, R. G. Woodbridge, Jr.

H. G. Sidebottom, *Secretary*

PHILADELPHIA SECTION.

Regular meeting, Thursday, October 16. 1919.

Address, "Bubbles," by Lieutenant-Colonel Wilder D. Bancroft, Chairman Division of Chemistry and Chemical Technology of the National Research Council.

J. Howard Graham, *Secretary*.

PUGET SOUND SECTION.

The October meeting of the Section was held at Bagley Hall, University of Washington, October 29, 1919.

Program: "The Work of the Chemist in the Condensed Milk Industry with Special Reference to Recent Development in Laboratory Methods," by P. A. Cornelius.

Ray W. Clough, *Secretary, Pro tem.*

ROCHESTER SECTION.

95th meeting, Monday, October 20.

Dr. C. E. North, head of the Milk Survey in Rochester, presented a paper entitled, "The Milk Problem in Rochester and Elsewhere."

Met Monday evening, November 17.

Program: "Microstructure of Plain Carbon Steels and Some Defects Usually Encountered" (illustrated), by Wilbur B. Miller, of The Pfaudler Co.

The 98th meeting was held December 1, 1919, Eastman Building, University of Rochester. Dr. Charles L. Parsons, Secretary of the American Chemical Society, presented an illustrated paper entitled, "The Nitrogen Situation."

E. M. BILLINGS, *Secretary.*

SAINT LOUIS SECTION.

The October meeting was held Monday, October 6, 1919. The following papers were presented: "Baking Powder Chemicals," by Mr. J. T. Meckstroth, of the Provident Chemical Works; "How Have the U. S. Chemical Manufacturers Met the Dyestuff Situation?" by Mr. F. S. Bacon, of Monsanto Chemical Works.

The November meeting was held Monday, November 3, 1919.

Program: "The Synthesis of Carbohydrates in the Plant," by Mr. F. W. Muncie, of Monsanto Chemical Works.

T. B BALL, *Secretary.*

SYRACUSE SECTION.

The October meeting of the Syracuse Section was held on Friday evening, October 24.

Major R. A. Baker, Professor of Chemistry at Syracuse University, spoke on "The Chemical Welfare Service Training Division."

J M JOBLIN, *Vice President*

The Syracuse Section of the American Chemical Society has decided to hold two meetings per month this year. The first November meeting was held on Friday evening, Nov. 14.

Mr. G. N. Berry spoke on his oversea's experiences. Mr. Berry visited the battlefields of France and industrial centers of England, observing particularly the labor conditions of the two countries.

R V. TOWNSEND, *Secretary*

TOLEDO SECTION.

The October meeting of the Toledo Section of the American Chemical Society was held on Monday, October 13, at 8.00 o'clock. Colonel Alfred H. White took for his subject, "The Fixation of Nitrogen."

A. B. CARNEY, *Secretary.*

UNIVERSITY OF ILLINOIS SECTION.

The 105th regular meeting was held Tuesday, November 18. Dr. C. W. Blake, formerly head of the Division of Inorganic Chemistry at the University of Illinois, now of the Fansteel Company of North Chicago, gave the address of the evening.

The 104th regular meeting of the Section was held Tuesday, October 21, 1919.

Dr. Irving Langmuir, of the General Electric Company, gave the address of the evening on the subject, "Structure of the Atoms and its Bearing on Chemical Valence."

S. A. BRALEY, *Secretary.*

UNIVERSITY OF MICHIGAN.

A meeting of the University of Michigan Section of the American Chemical Society was held on Tuesday, October 28.

Professor A. H. White gave a lecture on the subject of "The Fixation of Nitrogen." R. J. Carney, *Secretary.*

UNIVERSITY OF MISSOURI SECTION.

The University of Missouri Section of the American Chemical Society met Friday, October 24, 1919.

Program: Dr. H. D. Hooker, Jr., on "Effects and Treatment of Gas Poisoning."

VIRGINIA SECTION.

The first meeting of the fall was held Friday, October 17.

Program: Dr. Edgar Graham, Professor of Chemistry at University of Virginia, had for his subject, "Some Phases of the Problems of Fixation of Nitrogen." E. C. L. Miller, *Secretary*

WASHINGTON SECTION.

Regular Meeting.—The 295th meeting of the Society was held on Thursday, October 9, 1919.

Program: E. K. Nelson, Bureau of Chemistry, "Vanillyl Acid Amides." C. O. Johns and A. J. Finks, Bureau of Chemistry, "Growth Experiments with the Proteins of the Navy Bean." L. L. Steele and F. M. Washburn, Bureau of Standards, "A New Hexabromide Method for Linseed Oil." W. M. Clark and H. F. Zoller, Bureau of Animal Industry, "Manufacture of Commercial Casein."

Special Meeting.—The 296th meeting of the Society was held October 23, 1919.

Program: Charles L. Reese, Chief Chemist, du Pont Co., "Status and Prospects of the Dye Industry in the United States."

The 297th meeting was held at the Cosmos Club, November 13, 1919. The following program was given:

E. T. Wherry, Bureau of Chemistry, "Crystallography in the Service of the Chemist," (illustrated). E. T. Allen, Geophysical Laboratory, "A Few Methods for the Study of Fumaroles." (Dr. Allen recently returned from the National Geographic Society's expedition to Mt. Katmai.)

The following were elected officers for the year 1920: *President,* C. O. Johns; *Secretary,* E. C. McKelvy; *Treasurer,* F. P. Dewey; *Councilors,* R. B. Sosman, F. W. Smither, F. B. Power, A. Seidell, W. D. Collins. *Executive Committee,* R. C. Wells, P. B. Dunbar, M. J. Ingle, F. C. Cook, L. H. Adams, W. W. Skinner.

WESTERN NEW YORK SECTION.

The Western New York Section was addressed on October 28, by Mr. John E. Pennie on the subject of "Patent Laws with Special Reference to the Work of the Peace Commission." E. K. Strachan, *Secretary.*

WISCONSIN SECTION.

The October meeting of the Section was held on Wednesday, October 22, 1919.

Mr. W. G. Wilcox, of the Powdered Coal Engineering and Equipment Company, spoke on "The Essential Problems in the Successful Application of Powdered Coal."

The November meeting of the Section was held on Wednesday, November 12, 1919.

Dr. A. S. Loevenhart, Professor of Pharmacology and Toxicology, spoke on "The Biological and Medical Aspects of the Chemical Warfare Service."

JOHN H. SCHMIDT, *Secretary.*

DECEASED.

Raley, Hiram S., Riverton, Conn. Died June 3, 1919.
Graves, George H., New York City. Died August, 1919.
Drew, Harry, Easton, Pa. Died July 2, 1919.
Kreiser, Walter W., Jersey City, N. J. Died Oct. 11, 1919.
Hazelrigg, Virgil T., Oklahoma City, Died October 2, 1919.
Lyman, E. R., Edmunds, Wash., Died July, 1919.

VOL. XLI. JULY, 1919. NO. 7.

THE JOURNAL

OF THE

American Chemical Society

with which has been incorporated the

American Chemical Journal

(Founded by Ira Remsen)

[CONTRIBUTION FROM THE NEW YORK STATE COLLEGE OF FORESTRY AND SYRACUSE UNIVERSITY.]

ON THE QUINONE-PHENOLATE THEORY OF INDICATORS.[1] A SPECTROPHOTOMETRIC METHOD FOR MEASURING THE CONCENTRATIONS OF THE QUINOIDAL AND LACTOIDAL SALTS AND THE EQUILIBRIUM AND AFFINITY CONSTANTS OF THE PHENOLPHTHALEINS AND PHENOLSULFONPHTHALEINS.

BY R. T. BIRGE AND S. F. ACREE.

Received August 26, 1918.

The quinone-phenolate theory[2] postulates that phenolphthalein and phenolsulfonphthalein indicators, with both phenol groups alike, exist in solutions in the following equilibrium. The equations for indicators with unlike phenols, and with a hydrated form, $HOOCC_6H_4C(OH)(C_6H_4OH)_2$, will be given in the general theoretical article now completed.

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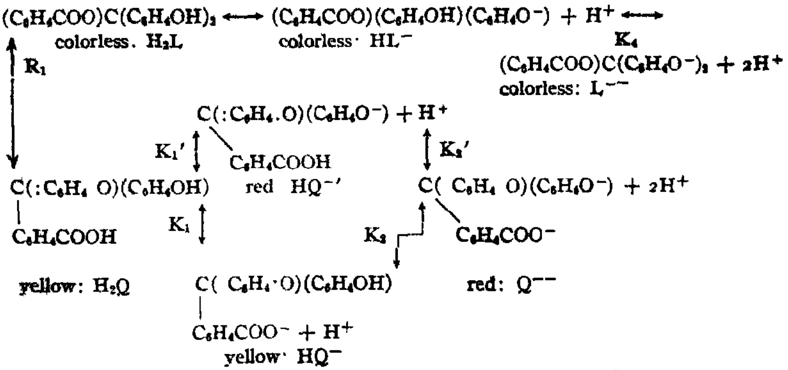
[1] This article is one of a series which we are publishing from the New York State College of Forestry at Syracuse University in coöperation with Dr. Haven Metcalf, in charge Forest Pathology, Bureau of Plant Industry, Dept. of Agriculture, on quantitative studies of the various chemical and physical factors governing the growth of fungi on culture media and trees.

[2] *Am. Chem. J.*, **37**, 71 (1907); **38**, 1 (1907); **39**, 528 (1908); **42**, 115 (1909); THIS JOURNAL, **38**, 2772 (1916); **39**, 648 (1917); **40**, 1092 (1918); *Science*, **42**, 101 (1915).


$(C_6H_4COO)C(C_6H_4OH)_2 \longleftrightarrow (C_6H_4COO)(C_6H_4OH)(C_6H_4O^-) + H^+ \longleftrightarrow$
colorless. H_2L
colorless· HL^-
K_4
$(C_6H_4COO)C(C_6H_4O^-)_2 + 2H^+$
colorless: L^{--}
R_1
$C(:C_6H_4.O)(C_6H_4O^-) + H^+$
K_1'
C_6H_4COOH
K_2'
$C(:C_6H_4\ O)(C_6H_4OH)$
red $HQ^{-'}$
$C(\ C_6H_4\ O)(C_6H_4O^-) + 2H^+$
C_6H_4COOH
K_1
K_2
$C_6H_4COO^-$
yellow: H_2Q
$C(\ C_6H_4{\cdot}O)(C_6H_4OH)$
red: Q^{--}
$C_6H_4COO^- + H^+$
yellow· HQ^-

We have found that $HQ^{-'}$ and Q^{--} give a strong absorption band in the green at about $1/\lambda = 1800$. In other words an intense red color is transmitted by $HQ^{-'}$ and Q^{--}, a faint yellow color is transmitted by solutions of H_2Q and HQ^-, while H_2L, HL^- and L^{--} are colorless.

From the ionization and equilibrium equations for such tautomeric[1] compounds,

$$\frac{H \times HQ^-}{H_2Q} = K_1 \quad (1) \qquad \frac{H \times HQ'^-}{H_2Q} = K_1' \quad (2) \qquad \frac{H \times Q^{--}}{HQ^-} = K_2 \quad (3)$$

$$\frac{H \times Q^{--}}{HQ'^-} = K_2' \quad (4) \qquad \frac{H \times HL^-}{H_2L} = K_3 \quad (5) \qquad \frac{H \times L^{--}}{HL^-} = K_4 \quad (6)$$

$$\frac{H_2L}{H_2Q} = R_1 \quad (7).$$

By simple algebraic combination of two or more of these equations, we may obtain the equilibrium ratio between any one (or several) of the above forms (ions or molecules) and any other (or several other) forms. Certain of the more interesting of these ratios are given below, the important ratios being indicated for convenience by a new constant.

$$\frac{(H)^2 \times Q^{--}}{H_2Q} = K_1K_2 = K_1'K_2' = \frac{(H)^2 \times Q^{--} \times R_1}{H_2L} \qquad (8)$$

$$\frac{(H)^2 \times L^{--}}{H_2L} = K_3K_4 \qquad (9)$$

$$\frac{(H)^2 \times Q^{--}}{(H_2Q + H_2L)} = \frac{K_1K_2}{1 + R_1} \quad (10) \qquad \frac{(H)^2 \times L^{--}}{(H_2Q + H_2L)} = \frac{K_3K_4R_1}{1 + R_1} \quad (11)$$

$$\frac{H \times (HQ^- + HQ'^- + HL^-)}{(H_2Q + H_2L)} = \frac{K_1' + K_1 + R_1K_3}{1 + R_1} = M_1 \quad (12a)$$

$$\frac{H \times (Q^{--} + L^{--})}{(HQ^- + HQ'^- + HL^-)} = \frac{K_1K_2 + R_1K_3K_4}{K_1' + K_1 + R_1K_3} = M_2 \quad (12b)$$

$$\frac{(H)^2 \times (Q^{--} + L^{--})}{(H_2Q + H_2L)} = \frac{K_1K_2 + R_1K_3K_4}{1 + R_1} = M_1M_2 \quad (12c)$$

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[1] *Am. Chem. J.*, 37, 71 (1907); 38, 1 (1907); 39, 528 (1908); 42, 115 (1909); THIS JOURNAL, 38, 2772 (1916); 39, 648 (1917); 40, 1092 (1918); *Science*, 42, 101 (1915).

The three Equations 12*a*, 12*b*, 12*c* give the "effective" ionization constants[1] (M_1 and M_2) obtained when one ignores the tautomerism, and considers simply the molecular, monovalent and divalent forms. Thus M_1 corresponds to K_1K_1' or K_3, while M_2 corresponds to K_2, K_2' or K_4. Similarly M_1M_2 corresponds to $K_1K_2 = K_1'K_2'$ or to $K_3K_4R_1$.

Equations 8 to 12*c* all involve a ratio between different steps of ionization, and so (H) or (H)^2 occurs in each equation. The following equations give some of the more interesting ratios where only one step of ionization is involved:

$$\frac{\mathrm{L}^{--}}{\mathrm{Q}^{--}} = \frac{R_1K_3K_4}{K_1K_2} = R_3 \quad \text{or} \quad \frac{R_3}{R_1} = \frac{K_3K_4}{K_1K_2} \tag{13}$$

$$\frac{\mathrm{L}^{--}}{\mathrm{Q}^{--} + \mathrm{L}^{--}} = \frac{R_3}{R_3 + 1} \quad (14a) \qquad \frac{\mathrm{Q}^{--}}{\mathrm{L}^{--} + \mathrm{Q}^{--}} = \frac{1}{R_3 + 1} \quad (14b)$$

$$\frac{\mathrm{HL}^-}{\mathrm{HQ}^-} = \frac{R_1K_3}{K_1} = R_2 \quad \text{or} \quad R_2/R_1 = K_3/K_1 \tag{15}$$

$$\frac{\mathrm{HL}^-}{\mathrm{HQ}'^-} = \frac{R_1K_3}{K_1'} = R_2' \quad \text{or} \quad R_2'/R_1 = K_3/K_1' \tag{16}$$

$$\mathrm{HQ}'^-/\mathrm{HQ}^- = K_1'/K_1 \tag{17}$$

$$\mathrm{HQ}'^-/\mathrm{Q}^{--} = \mathrm{H}K_1'/K_1K_2. \tag{18}$$

The general method of measuring the absorption *at different frequencies* in the visible and ultraviolet regions, and at successive stages of neutralization to learn the amounts of the several salts present, was proposed in lectures and articles at various times from 1908 to the present. The plan was suggested for use with colored indicators and also with such tautomeric compounds as the colorless urazoles whose absorption spectra would be studied in the ultraviolet.[2] Schaeffer, Paulus, Hutchinson and Jones[3] measured the absorption at different frequencies by means of an improved suspended thermocouple method developed by Professor A. H. Pfund and Dr. J. S. Guy. Their studies substantiated the applicability of the theory in the best work yet published on rosolic acid, phenolphthalein and methyl orange. Pfund, Uhler, Anderson, Jones and Wood[4] had also used the photographic methods in the visible and ultraviolet in other studies, and Uhler and Wood photographed the spectra of a number of dyes. Hildebrandt[5] had used a spectrophotometer with phenolphthalein but made measurements at just one frequency in the red. Dr. H. A. Lubs prepared urazole esters and salts in 1914 for the investigations as a part of his dissertation but did not have time to undertake the spectrophotometric measurements. These studies in the urazole series will now be continued.

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[1] The method of derivation of 12*a*, 12*b*, 12*c* and other similar complex equations will be discussed in the long theoretical article now ready for publication.

[2] See *Am. Chem. J.*, 42, 123 (1909) and all of our more recent articles.

[3] THIS JOURNAL, 37, 776, 1694 (1915).

[4] Carnegie Publications.

[5] *Z. Elektrochem.*, 14, 351 (1908).

In the quantitative use of indicators for measuring the acidity of solutions, as in studying reaction velocities or the growth of fungi on culture media, it becomes imperative to know the magnitude of the above constants and to vary them at will by introducing substituent groups which will make the indicators extremely sensitive and useful over a wide range of hydrogen ion concentration. In this article, therefore, we shall discuss especially the equilibrium and affinity constants and their relation to the intensity of the colors of various indicators at different hydrogen ion concentrations.

It is obvious that these constants and ratios can vary widely with different substituent groups and we therefore have a means of preparing different series of indicators that will (*a*) give varying intensities for definite equivalents of alkali and, (*b*) give their color changes at the different hydrogen ion concentrations or P_H values. Up to this time it has not been possible for us to calculate with any certainty the relative concentrations of the colorless lactoidal, yellow quinoidal, and deeply colored quinone-phenolate salts in the acid or alkaline solutions of the phenolphthalein series. We did know from White's synthetic, conductivity and spectroscopic work[1] and Lubs'[2] P_H values that the phenolsulfonphthaleins exist practically only as quinone-phenolates in alkaline solutions and consequently give brilliant color changes. But our own, and Guy's unpublished (finished 1916) spectrophotometric measurements and those of Howe and Gibson[3] now give us sufficient insight into the phenomena involved to enable us to begin to measure or calculate (*a*) the concentrations of the lactoidal (H_2L) and of the quinoidal (H_2Q) free indicator, (*b*) the colorless lactoidal mono- (HL^-) and dibasic (L^{--}) salts, (*c*) the yellow quinoidal mono-basic salt (HQ^-), (*d*) the deeply colored mono-basic quinone-phenolate salt (HQ'^-), and (*e*) the deeply colored dibasic quinone-phenolate salt (Q^{--}) of all indicators of this general type.

This is such a very important advance in the history of the study of the indicators that the results will now be outlined, together with some plans for future work on these tautomeric compounds.

Discussion of the Phenolsulfonphthalein Series.

In order to aid the reader in following the discussion it may be well to summarize the meaning and probable values of the various constants defined by Equations 1 to 7.

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[1] White and Acree, New Orleans Address, *Science*, 42, 101 (1915) THIS JOURNAL, 39, 648 (1917); 40, 1092 (1918)

[2] Lubs and Acree, *Ibid.*, 38, 2772 (1916), Lubs and Clarke, *J. Wash. Acad. Sci.* 5, 609 (1916); 6, 483 (1917). *J. Bact.*, 2, 1, 109, 137 (1917)

[3] *Phys. Rev.*, 10, 767, 779 (1918)

(*a*) R_1 gives the equilibrium between the lactoidal and quinoidal forms. Our work seems to indicate a value of about 1000 for phenolphthalein and of about unity for phenolsulfonphthalein.

(*b*) K_1 and K_2' refer to the ionization constants of the sulfonic acid residue in phenolsulfonphthalein, or to the phthalic acid residue in phenolphthalein. They are very large, about 10^{-1}, for phenolsulfonphthalein, and about 10^{-5} or 10^{-4} for phenolphthalein.

(*c*) K_1' and K_3 refer to a primary phenol ionization. They are both very small, and probably of about the same order of magnitude, say 10^{-8} to 10^{-10}, for phenols with no negative or positive substituent groups. The introduction of positive or negative groups into the phenol radical decreases or increases K_1' and K_3.

(*d*) K_2 and K_4 refer to a secondary phenol ionization. They are therefore still smaller than K_1' and K_3.

Equation 13 shows that in a series of indicators having the same absorption index for unit equivalent of quinone-phenolate ions, those indicators having the *largest* values of K_1K_2 and *smallest* values of $R_1K_3K_4$ should give the largest value Q^{--}/L^{--}, and the greatest absorption in the green and consequently the most intense transmitted red color. For that reason we chose the sulfonphthalein series with a large value for K_1, about 10^{-1}, for the sulfonic acid group, with a *small* value for R_1, about 10 or less, and with K_2, K_3 and K_4 variable at will, as being one of the most promising groups of indicators for practical use as well as for the study of the general theory. The small ratio R_1 enables us to study the properties of the actual yellow quinoidal form, H_2Q (which is not present in appreciable quantities in the phenolphthalein series), and of the monobasic yellow salts corresponding, KHQ, which have been made and described by White[1] (and which have not been *isolated* in the phenolphthalein series but which we shall measure spectrophotometrically in the alkaline solutions). The value of K_1 is so large in comparison with R_1K_3, K_2 and K_4 in the phenolsulfonphthalein that well over 90% of the indicator is titrated as a yellow quinoidal monobasic acid before the "turning point" or intense color change appears. To illustrate, to state that K_1 is large in comparison with R_1K_3 means from Equation 15 that little of the monovalent ions are lactoidal and colorless (HL^-). When K_4 is small in comparison with K_1, and R_1K_3 is likewise small, Equation 13 shows that little of the divalent ions are lactoidal and colorless (L^{--}). When K_2/K_1 is small, and R_1K_3 and K_4 are also small, Equations 1 and 3 give by division $K_2/K_1 = \dfrac{(H_2Q) \times (Q^{--})}{(HQ^{--})^2}$, which shows that no appreciable quantity of (Q^{--}), *the red salt*, can be formed while there is appreciably any unchanged indicator (H_2Q) remaining in solution with the affinity constant of phenol is approximately 10^{-10} at 25°, whereas that of *o*-chlorophenol is 7.7×10^{-10}, that of *o*-nitrophenol is 700×10^{-10}, that of 2,4,6-trichlorophenol is 260×10^{-10}, and that of 2,6-dinitrophenol is $2{,}700{,}000 \times 10^{-10}$. It is clear then that the introduction of these negative groups into the phenolic radicals of the sulfonphthalein series will very greatly increase K_3. K_2 and K_4 are both secondary ionization constants arising from the phenol groups and their values will also be greatly increased. As they will both be enlarged in a similar manner and as the data on the secondary ionization constants of dibasic acids show that the ratio K_2/K_4 will not vary to any extent comparable with the change in K_3, it is clear that the per cent of lactoidal salt or $L^{--}/(Q^{--} + L^{-})$ will be increased *manifold* by the introduction of the negative groups and is chiefly governed by K_3/K_1, R_1 apparently changing very little in comparison. If, however, in phenolsulfonphthalein $R_1K_3K_4/K_1K_2$ were of the order $10^{-10}/10^{-1} = 10^{-9}$ it is clear that this value could be increased a *million fold*, or 10^6 fold, and there would still be only 10^{-3} or 0.10% of the lactoidal salt and hence 99.9% of the quinone-phenolate salt in the alkaline solution. While K_3/K_1 is increasing K_2 is becoming larger in the desired degree illustrated in the following examples,[1] the P_H range of course decreasing. Phenolsulfonphthalein has a useful indicator range corresponding to P_H values of 6.50 to 8.50, and a K_2 of about 2.0×10^{-8}. The introduction of isopropyl groups in the thymolsulfonphthalein raises this P_H range to 8.0–9.5. The introduction of two bromines into the thymolsulfonphthalein lowers the P_H range to 6.0–7.6. Two bromines and two methyls in the ortho positions in dibromo-*o*-cresolsulfonphthalein lower the P_H range to 5.2–6.8, whereas 4 bromines in tetrabromophenolsulfonphthalein lower the P_H range to 2.8–4.6. The 4 nitro groups in tetranitro-phenolsulfonphthalein lower the P_H range to <2.0. The introduction of a nitro group into the benzenesulfonic radical of phenolsulfonphthalein and thymolsulfonphthalein increases K_1 but does not appreciably change K_2 for the phenolic group and hence the P_H ranges 6.8–8.4 and 8.0–9.5, respectively, remain unchanged. These different indicators give color changes, then, at P_H ranges varying from about 10 to <2, the K_2 values increasing simultaneously, and in all cases the color changes are *brilliant* because practically all of the indicator is in the deeply colored quinone-phenolate form and very little is in the colorless lactoidal form. These satisfactory results were predicted from the theory just as the *low color intensities* of the corresponding halogenated phenolphthaleins observed by Howe and Gibson were forecast.

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[1] Reference to article now in editor's hands.

One other point is predicted and will be studied. The introduction of negative groups into the phenol groups will increase very greatly (and by about the same factor) the primary phenol ionization constants K_1' and K_3 and the secondary phenol constants K_2 and K_4 without appreciably altering K_1. It therefore follows that the *color intensity* $\left(\text{given by } \frac{Q^{--}}{L^{--} + Q^{--}} = \frac{K_1K_2}{R_1K_3K_4 + K_1K_2}\right)$ will be lowered, since K_2, K_3 and K_4 in the denominator increase, while only K_2 in the numerator increases. But at the same time a greater portion of the intense color will come from HQ'^{-}. For the ratio of HQ'^{-} to all quinoidal form is given by

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[1] Lubs and Acree, This Journal, 38, 2772 (1916); Lubs and Clark, *J. Bact.*, 2, 114.

$$\frac{HQ^{-'}}{H_2Q + HQ^{-} + HQ^{-'} + Q^{-}} = \frac{K_1'}{H + K_1 + K_1' + K_2K_1/H} \qquad (21)$$

In this expression, the numerator increases directly, under the above condition, while the denominator (of which K_1 is the largest term, except for *very* small H) increases less rapidly than in a direct ratio. For sufficiently small H, practically all the intense red color must of course come from Q^{-}, regardless of the probable values of the various constants, but for all intermediate values of H the $HQ^{-'}$ will thus play a more and more important role, as negative groups are introduced into the phenol group. Also, $HQ^{-'}$ *decreases* as the first power of the hydrogen ion concentration *increases*, while Q^{--} changes with the second power of the hydrogen ion concentration. We thus have a ready means of determining the relative concentrations of $HQ^{-'}$ and Q.

This same theory shows why the introduction of negative chloro, bromo, etc., atoms into the phenolic groups of phenolphthalein and of phenoltetrachlorophthalein still further and very greatly lowers the color intensity of these indicators in alkaline solution. The proof of the theory has now been developed by an interpretation of the fine work of Howe and Gibson on the phenolphthalein series, which will now be discussed.

Discussion of the Phenolphthalein Series.

Howe and Gibson[1] have observed, in an excellent study by a combination of visual and photographic methods, the complete absorption curves in neutral and alkaline solutions of seven substances of the phenolphthalein series of indicators and of phenolsulfonphthalein, all of the chemicals having been prepared by Professor W. R. Orndorff and Dr. S. A. Mahood. The absorption curves were determined from about 2000 Å. in the ultraviolet to 6500 Å. in the red. The curves show that all of these substances in the free state possess the expected lactoidal phenolic absorption bands in the ultraviolet, even if they have none in the visible spectrum. In this article however we are concerned with these substances chiefly in relation to their use as indicators. We shall therefore discuss fully only the green band centering at about $1/\lambda = 1800$ and arising from the quinone-phenolate group. This band grows up in alkaline solution with increasing quantities of added base and its presence and magnitude is practically the sole determining factor. The band $1/\lambda = 2700$ in the ultraviolet arising from the quinone-phenolate group will change along with the green band. Both of these bands are present, either more or less sharply or merged together, in the alkaline solutions of aurine, rosolic acid, tetrabromorosolic acid, fluorescein and its derivatives, phenolsulfonphthalein and its derivatives, alizarine, and a large number of other compounds whose color changes have been shown[1] by spectrophotometric methods to arise from the quinone-phenolate group. If both of these bands come solely from the quinone-phenolate group we should expect them to be formed in constant ratio from any given indicator as more and more alkali is added, and we might even expect different indicators of the same general type to give comparable ratios from these two bands. Of course, we should expect the position and ratio of these bands to vary to some extent with different substituent groups, as Howe and Gibson discussed. Furthermore there is a general absorption in the ultraviolet which masks the bands and makes any conclusions valuable only as first approximations. That there is a *general* constancy for this ratio is shown in the following Table I which was calculated from the data of Howe and Gibson by Professor C. L. Brightman who is now coöperating with us in this work. Both of these bands should be measured and compared accurately for a large number of these indicators to test the theory, but in all practical use of the indicators the large green band is the one most easily studied by spectrophotometric methods.

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[1] *Loc. cit.*

We have also hoped that the phenolate ions of the colorless lactoidal salts will show characteristic bands in the ultraviolet whose magnitude and position will enable us to measure the concentration of such ions. It seems to us that the data of Howe and Gibson do not permit us to draw definite conclusions as to whether the ultraviolet band at about $1/\lambda = 3200$ is connected with the phenolate ions (as against carboxylate or sulfonate salts). If such proves to be the case and accurate measurements can be made we shall then be able to study carefully the concentrations of the free lactoidal form, the lactoidal phenolate ions, the quinoidal form and its salts, and the quinone-phenolate ions, and hence we will be able to measure the tautomeric equilibrium and affinity constants of all these substances. Howe and Gibson make no attempt to interpret their data in this respect. As a matter of fact, it is impossible to interpret the data without the use of certain general equations which we have developed fully.

The 7 phenolphthaleins used by Howe and Gibson are: Phenolphthalein, tetrachloro-phenolphthalein, tetrabromo-phenolphthalein, tetraiodo-phenolphthalein, phenoltetrachloro-phthalein, tetrabromo-phenoltetrachloro-phthalein, tetraiodo-phenoltetrachloro-phthalein. These substances are but slightly soluble in aqueous, non-alkaline, solution. They therefore used them in alcoholic solution with no alkali, and then with 2, 4, and 10 molecules of alkali. They also obtained curves in aqueous solution with 4 to 10 mols of added alkali. They give no curves for the free acid in aqueous solution, doubtless because of the small solubility.

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[1] See the first article by White and Acree, THIS JOURNAL, 40, 1092 (1918), and work appearing later by Professors Guy and Brightman in coöperation with us.

TABLE I

	Aqueous solution				Alcoholic solution			
Indicator	Mols of alkali	Absorption Index B $1/\lambda = 1800$	Absorption Index B' $1/\lambda = 2700$	Ratio B/B'	Mols of alkali	Absorption Index B $1/\lambda = 1800$	Absorption Index B' $1/\lambda = 2700$	Ratio B/B'
Phenolphthalein	10	2.7	0.47	5.84	10	0.7	0.12	5.83
Tetrachloro-phenolphthalein	*	*	*	*	*	*	*	*
Tetrabromo phenolphthalein	*	*	*	*	*	*	*	*
Tetraiodo-phenolphthalein	*	*	*	*	*	*	*	*
Phenoltetrachloro-phthalein	4	5.85[d]	0.8	7.18	2	1.4	0.3	4.6
					4	2.6	0.5	5.2[a]
					10	4.0	0.85	4.7
Tetrabromo phenoltetrachloro-phthalein	10	1.0	0.15	6.65	*	*	*	*
Tetraiodo-phenoltetrachloro phthalein	4	2.4	0.25	9.6	*	*	*	*
Phenolsulfonphthalein	1.5	3.6	0.65	5.54	10	5.2	0.80	6.5[b]
	2.0	4.4	0.75	5.86	10	5.2	0.5	10.4[c]

In the case of the phenolsulfonphthalein series of indicators, which the present authors are studying in detail, it is possible to obtain aqueous, non-alkaline solutions, and to observe accurately the gradual change in absorption spectrum as alkali, acid, or salt, is added. Howe and Gibson studied phenolsulfonphthalein by the titration method developed by White and Lubs[1] in cooperation with us for the entire sulfonphthalein series, and observed the absorption curves for 0, 1, 1.5, and 2 mols of added alkali. Their results check roughly with those of White (1915), Guy (1916), and the present authors (1917–18), which were obtained and interpreted before

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* In these cases the band was too weak to give a good value of the index on the curve.

[a] This calculation was made on the assumption that the D curve in the ultraviolet and the O curve in the visible regions are for the same solution.

[b] Calculated from the total heights of the bands.

[c] Calculated from the increased heights of the bands.

[d] The reading in Fig. 6, p. 772, corresponds to about 5.85, whereas Howe and Gibson give 5.95 in Fig. 8. This and other similar discrepancies are too small to warrant discussion.

[1] *Loc. cit.*

the article by Howe and Gibson appeared, and which will be discussed in full in another article. We will here consider only the interpretation of the results for the 7 phenolphthalein compounds mentioned above.

All of these indicators are dibasic, tautomeric acids, and their behavior depends on the relative magnitudes of the various affinity constants of the acid radicals and upon the equilibrium constants. In the preceding section on sulfonphthaleins we concluded that adding chloro, bromo, nitro, etc., to the phthalic acid residue strengthens this group but does not appreciably affect the strength of the acid phenolic group, the phenolsulfonphthalein and phenolnitro-sulfonphthalein having the same P_H range 6.8 - 8.4 and thymolsulfonphthalein and thymolnitro-sulfonphthalein having about the same P_H range, namely, about 8.0 to 9.5. But adding bromo and iodo groups to the phenol residue raises the phenolic affinity constant without appreciably disturbing the K_1. When at the same time chloro groups are added to the phthalic acid residue, and chloro, bromo or iodo groups to the phenol residue, the same general relations can be roughly predicted.

Now according to the quinone-phenolate theory, the intensity of this green band, which is present in all of these compounds, is a measure of the amount of quinone-phenolate ion present. In very dilute solutions the quinone-phenolate salt can be considered as practically completely ionized, especially if the molecular salt is also assumed to have the same color. This red ion is formed from the yellow quinoid, H_2Q, as has been shown in the preceding articles, and can exist in the two forms HQ'^- (quinoidal-phenolate primary ion) and Q^{--} (quinoidal-phenolate secondary ion). We can assume as a first approximation that if *all* of the indicator were in the form Q^{--}, for high alkalinity, the intensity of the green band (at its center point) would be nearly the same for all substances of the phenolphthalein and phenolsulfonphthalein series of indicators. This assumption is based on experimental facts which will be developed in the following.

Let us, as before, assume equilibrium between the molecular lactoidal and quinoidal form $(H_2L)/(H_2Q) = R_1$.

Then, as shown, the equilibrium between the dibasic ions is given by $L^{--}/Q^{--} = R_3 = R_1K_3K_4/K_1K_2$ (13).

For high acidity the ratio of all lactoidal to all quinoidal forms is given by R_1, for high alkalinity by R_3. This has been shown in Equations 7 and 13. The phenolphthalein, as a free acid, is colorless and is therefore considered to exist almost entirely in the colorless lactoidal form. Certainly the absorption is hardly more than the experimental errors involved in the measurements, namely at least 0.1 or 0.2%. Therefore R_1 is large. Furthermore, an analysis of the work of Rosenstein, together with that of Howe and Gibson, indicates that R_1 is 10^3 or greater, also that K_1 is of the order 10^{-6} and K_2 is about 10^{-9}. K_3 and K_4 must be of the same order and $R_3 = L^{--}/Q^{--} = R_1K_3K_4/K_1K_2$ can easily become $R_3 = 1$, as shown below by the experimental data. If $R_3 = R_1K_3K_4/K_1K_2 = 1$ it follows that the introduction of halogens into the phenol groups will increase K_3K_4/K_2 very greatly, say from 10 to 10^2 fold, without changing K_1 materially. If we assume[1] for the moment that R_1 remains constant it follows that L^{--}/Q^{--} must increase 10 to 10^2 fold and that the per cent. of quinone-phenolate salt must decrease to a value of from 10 down to 1%. In other words, the indicator will be practically lactoidal and faintly colored in alkaline solution. That this theory is correct is shown in Table II where it is seen that not over 2% of the tetrachloro-, bromo-, or iodophenolphthalein forms the quinone-phenolate salt in alkaline solution. If on the other hand, K_1 is made larger by the 4 chlorines in phenoltetrachloro-phthalein and R_3 becomes 1/10 as large as for phenolphthalein, then 90% or more of the phenoltetrachloro-phthalein would be in the quinone-phenolate form in alkaline solution. This is shown in Table II below. The introduction of halogens into the phenol groups of phenoltetrachloro-phthalein would then raise the value of R_3, as above, and decrease the per cent. of quinone-phenolate salt to the 17 and 40% given for tetrabromo-phenoltetrachloro-phthalein and the tetraiodo compound in Table II. The halogen derivatives of phenoltetrachloro-phthalein have therefore a greater specific color intensity than the corresponding ones of phenolphthalein but a smaller specific color intensity than the corresponding phenolsulfonphthalein derivatives. We thus have three classes of indicators giving a wide range of per cent. of quinone-phenolate salt in the alkaline solution, the determining factors most apparent being the different values for R_1 and the increasing value of K_1 for the phthalic acid, tetrachloro-phthalic acid, and phenolsulfonic acid residues. These classes will give interesting measurements.

For phenoltetrachloro-phthalein, we have the strongest phthalic acid group, and the relatively weakest phenol group. Therefore K_1 is much greater than the K_1 for the phenolphthalein and therefore proportionately greater than the K_3 of the phenoltetrachloro-phthalein and unless R_1 is very large, the substance will exist almost entirely in the quinoidal form, for high alkalinity. In aqueous solution and at high alkalinity the intensity of the green band for this substance, in the units used by Howe and Gibson, is 5.95. They found the intensity of the same band for phenolsulfonphthalein, which is known from our previous work to be practically entirely in the quinoidal form at high alkalinity, to be 4.50 with 2 mols alkali in water, and 5.2 with 10 mols alkali in alcohol. Howe and Gibson did not reach the true "end-point"[2] with phenolsulfonphthalein as it is necessary to add more than 2 mols alkali to do this with 0.0001 N aqueous solutions. The work of the present authors also shows that when all the substance is evidently in the quinoidal form, at high alkalinity, the intensity of the green band is approximately the same for various different indicators of the phenolsulfonphthalein series. We can at first therefore take 5.95 as an approximate *measure* of the intensity of this band when we have 0.000,1 N concentration of quinone-phenolate ions in a one cm. cell, the unit used by Howe and Gibson.

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[1] See the discussion of R_1 and R_3 on page 1047.

[2] By the "end-point" we mean obviously the stage of neutralization of the indi-

Then since for *phenolphthalein* the intensity in water is only 2.62, it indicates that only about $^1/_2$ *this indicator salt is in the quinoidal form, even for very high alkalinity.* This is contrary to the conclusion[1] of past investigators, but the very accurate data of Howe and Gibson and our own measurements allow of no other interpretation, so far as we can see. R_3 is therefore approximately unity, and it is difficult to see how it could be greater than two or less than 0.5. This fact, combined with Rosenstein's data (to be later discussed) yields the approximate values of the primary ionization constants given above.

All of the other substances used by Howe and Gibson can be similarly studied and interpreted. For tetrabromo-phenolphthalein the phenol affinity constant (K_3) is probably fully as large if not larger than K_1 and therefore if 1% is in the quinoidal form at the start (high acidity) only 1% or less will be in that form at the end (high alkalinity). The intensity of the band is 0.033 and so about 0.5% is in the quinoidal form at the end.

We have calculated Howe and Gibson's results in the following way: First, we have assumed a value 5.95 for the index of any indicator existing in any solvent entirely as the quinone-phenolate form. We have then used Howe and Gibson's data to calculate the per cent. of each indicator actually present in the quinone-phenolate form, Q^{--}, when varying quantities of alkali are added, the difference between unity and the per cent. of quinone-phenolate giving the per cent. of lactoidal dibasic colorless ion L^{--}. The ration $R_3 = L^{--}/Q^{--}$ is then readily calculated and is given for both alcohol and water in Table II, which was computed by Professor Bright-

cator at which the quinone phenol -C(.C_6H_4 O)(C_6H_4OH) (and its tautomer, if any) is fully converted into the corresponding quinone-phenolate ion (and its tautomer, if any). In measuring this "end-point" spectrophotometrically within any given experimental error a correction must be made for any unchanged quinone phenol (and tautomer, if any) and for any substance (such as the colorless hydrated salt) which is formed from the quinone-phenolate (or tautomer, if any) and whose concentration depends upon the concentration of the hydrogen (hydroxyl) ions or upon a "salt effect." See also Brightman, Hopfield, Meacham and Acree, THIS JOURNAL, **40,** 1940 (1918).

[1] For example, see an excellent discussion by A. A. Noyes, THIS JOURNAL, **32,** 816, 817 (1910).

man. As discussed below, Q^{--} is too small, and L^{--} is too large because it really involves the unchanged indicator, the colorless and yellow monobasic salts and any hydrated or alcoholated colorless salt. Consequently R_3 will probably be lowered in all cases when the true "end-point" for each substance is measured. The results for the aqueous solutions are probably much nearer the "end-point" than those for the alcoholic solutions.

It seems that the following preliminary conclusions can be drawn from the tables: First, as indicated in Table I, the addition of increasing quantities of alkali, up to 20 mols in some cases, increases the quinone-phenolate concentration and hence the absorption index, until the "end-point" is reached, at which all of the indicator is converted into the dibasic lactoidal and quinone-phenolate salts. Howe and Gibson followed the "titration method" of White[1] and found the greatest change in phenolsulfonphthalein between one and two mols of alkali in aqueous solution, which accords with the prior work of White and Guy and ourselves and with the theory. This gradual increase in absorption index with increase in alkali up to and beyond the "turning point" has been investigated very extensively with a number of sulfonphthalein indicators by

TABLE II.—PER CENT. OF VARIOUS INDICATORS IN QUINONE-PHENOLATE FORM IN ALKALINE AQUEOUS AND ALCOHOLIC SOLUTIONS.

Phenoltetrachloro-phthalein Taken as 100% Quinoidal in Aqueous Solution with an Absorption Index 5.95.

	Aqueous		Alcoholic				
Indicator	Mols alkali	% in quinone phenolate form	Mols alkali	% in quinone phenolate form	Aqueous R_3	Alcoholic R'_3	Ratio R'_3/R_3
Phenolphthalein	10	0.44	4	1.5			
			10	11.3	1.27	7.88	6.20
Tetrachloro phenolphthalein	4	0.354	10	0.0354	282	2820	10.0
Tetrabromo-phenolphthalein	4	0.555	10	0.095	180	1052	5.85
Tetraiodo-phenolphthalein	4	1.68	10	0.208	58.5	481	8.2
			2	23.5			
			4	43.3			
Phenoltetrachloro-phthalein	2	100 (by definition)	10	67.2	0	0.49	
Tetrabromo-phenoltetrachloro-phthalein	4	17	4	2.34			
			20	3.3	4.88	29.2	6.0
Tetraiodo-phenoltetrachloro phthalein...	4	40	5	4.58	1.50	20.6	13.7
Phenolsulfonphthalein	1	11.3	10	86.6			
	1.5	60.5					
	2	74.8					

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[1] *Loc. cit.*, see also Lubs and Acree, THIS JOURNAL, 38, 2772 (1916).

Professor J. S. Guy in 1916 in coöperation with our own work and has been used in calculating the affinity constants. Secondly, as far as we can judge until the indexes for the true "end-points" are measured, all of these tables and figures show clearly the following: the larger the ratio of K_1, the ionization constant for the carboxyl or sulfonic acid group, to K_3, the ionization constant of the first phenol of the lactoid form, the larger the absorption index and per cent. of quinone phenolate in the alkaline solution. The larger the values of K_3K_4 are made, in comparison with K_1K_2, by the introduction of negative groups into the phenolic residues (R_1 remaining constant), the larger the per cent. of lactoidal colorless salt in the alkaline solutions and the smaller the absorption index. It is hoped that in time methods for the direct measurement of the concentration of the lactoidal colorless salts will be developed and that more will be learned about R_1.

We see that Howe and Gibson's results for aqueous and alcoholic solutions are similar, but the R_3 (alc.) is in all cases larger than R_3 (aq.), and as the last column shows, the ratio R_3 (alc.)/R_3 (aq.) is not constant. But this result is not unexpected for the formation of the alcoholate and especially alcoholysis tend to prevent the "end-point" being reached unless a larger number of moles of alkali are added. But, as the data of Howe and Gibson show, 10 mols of alkali were added for the first indicators, but only 4 moles of alkali for the last 3 indicators. The concentrations used are also different for different indicators, and our results have shown that the number of moles of alkali necessary to reach the true "end-point" depends radically upon the concentration. Their curves show clearly that 4 and even 20 mols of alkali have not produced the full color change in alcohol and the ratios given for the last two indicators may be proportionately too large. With complete data it will be very important to study these ratios and the equilibrium and affinity constants in water, alcohol, acetone, etc., as we have proposed in an earlier article[1] to do. By determining the ion product $K_{alc} = H \times OC_2H_5$ for pure ethyl alcohol and using sodium, potassium and lithium ethylates it will be possible to measure the alcoholysis and affinity constants of a large number of weak acids (phenols, ketones, amines, etc.), many of which are insoluble in water.

Besides the changes of intensity of the green band, there is also the usual shift in position, due to loading down the molecule. Howe and Gibson discussed this shift and show that it increases with the atomic weight of the added group.

An examination of Equations 13 and 7 shows that we are now in a position to begin to calculate the values of R_1, R_3, and K_3K_4/K_1K_2 approximately from the experimental data on some of these constants instead of having to rely on the obviously weak assumption used above that R_1 does not change in some cases. The equations become $H_2L/H_2Q = R_1 = R_3K_1K_2/K_3K_4$ or $H_2Q = H_2LK_3K_4/R_3K_1K_2$. For colorless indicators of the phenolphthalein type, H_2Q is too small to be measured directly today. But H_2L is practically the concentration of the free indicator, R_3 can now be approximately measured by the methods outlined in this paper; by measuring K_1K_2/K_3K_4 we can calculate H_2Q and hence R_1. In the sulfonphthalein series we shall probably be able to measure R_1 and R_3, or one of its components, directly and hence secure better experimental data on all these constants.

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[1] *Am Chem. J.*, 39, 542 (1908), and later articles.

More light on the values of R_1 and R_3 is greatly needed. For example, the introduction of 4 bromines into the phenol groups of the phenolsulfonphthalein does not materially change the per cent. of Q^{--} in alkaline solutions, and the useful P_H range corresponding to K_2 is therefore *lowered greatly*,[1] from 6.5–8.5 to 2.8–4.6. But the introduction of 4 bromines into phenolphthalein lowers the midpoint of the P_H range from about 9 to only about 8, or only $^1/_4$ the change for phenolsulfonphthalein. This apparent discrepancy becomes clear from the equation for expressing the change of color with change in (*a*) concentration of the hydrogen ions and in (*b*) the equilibrium and ionization constants, which will be developed fully in a later article. The equation shows clearly that the hydrogen ion

$$(H\{H(K_1'R_3 - K_3R_1 - K_1)/(R_1 + 1)][\alpha'/(1 - \alpha')] = (K_1K_2 + K_1'H)(R_3 + 1)/(R_1 + 1) \quad (22)$$

concentration necessary to produce 50%[2] of the specific absorption index (or specific color intensity) depends not only on K_1, and on K_1', K_2, and K_3, which are ionization constants for phenols increased in strength by the bromines, but also on $(R_3 + 1)/(R_1 + 1)$. Considering the right side of the equation, we see that the P_H range can be *lowered greatly* by introducing the 4 bromines (as in tetrabromo-phenolsulfonphthalein) provided the *increases* in K_1' and K_2 are not offset by a *decrease* in $(R_3 + 1)/(R_1 + 1)$, or can be *lowered slightly* (as in tetrabromo-phenolphthalein) or even *increased*, provided a *decrease* in $(R_3 + 1)/(R_1 + 1)$ more than offsets *increases* in K_1, K_2 and K_3. We have seen from Table II that $(R_3 + 1) =$ about $(1.25 + 1.0) = 2.25$ for phenolphthalein becomes $(R_3 + 1) =$ about $(180 + 1) = 181$ for tetrabromo-phenolphthalein. This increase of 80-fold multiplied by 3,000,[1] the increase in the ionization constant K_3 for the phenolic group by the introduction of the 4 bromines, gives a change of say 240,000-fold[2] in the numerator and the $(R_1 + 1)$ must therefore increase 24,000-fold to balance the change of the hydrogen ion concentration from 10^{-9} for phenolphthalein to 10^{-8} for tetrabromophenolphthalein. The left side of the equation must be treated in the same way, and this example serves to illustrate the underlying ideas which will be applied later in detail. Since $(R_1 + 1)$ is already large for phenolphthalein, say 1000 or larger, an increase of 24,000 fold means simply that free tetrabromo-phenolphthalein has practically no quinoidal component in the aqueous or alcoholic solution.

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[1] Lubs, White and Acree, THIS JOURNAL, 38, 2779 (1916), 39, 649, 651 (1917); Lubs and Clark, *Loc. cit*

[2] 50% neutralization of the indicator by a base does not necessarily correspond to 50% of the specific absorption index. Thus 50% neutralization of phenolsulfonphthalein gives the yellow monobasic salt and only a few per cent of the dibasic quinone-phenolate salt, and it requires around 75% of neutralization to give 50% of the specific absorption index.

Our own absorption spectra, and those of Howe and Gibson, for phenolsulfonphthalein give further very important evidence on the question whether the quinone group remains free or combines[3] with the phenolate ion or salt to form intensely colored double compounds very much like those which Jackson[4] made by the union of quinones with phenol salts. The free sulfonphthaleins with nonionized phenols give an absorption band in the violet centering at about 2300 and another in the ultraviolet at 3770. The specific absorption index for the violet band [apparently about two for phenolsulfonphthalein] will be used in this entire series for measuring the per cent. of free quinoidal acid, H_2Q. This violet band practically disappears in alkaline solution and new bands are formed at about 1800, 2800 and 3500. It therefore seems certain that the quinone group, or quinonephenol group, $—C(:C_6H_4:O)(C_6H_4OH)$, disappears and is changed into the quinone-phenolate group, $—C(:C_6H_4:O)(C_6H_4OK)$, as described in the earlier articles. This phase of the theory needs and will receive very close attention.

In the above calculations it was assumed that the colorless salts are lactoidal, and not hydrated (alcoholated in alcohol) tribasic salts $KOOCC_6H_4C(OH)(C_6H_4OK)_2$. The fine work of Kober and Marshall[5] on the fading of phenolphthalein shows that an excess of alkali causes quick fading of the color and that the final intensity varies inversely as the concentration of the free alkali. Since Howe and Gibson doubtless used the most refined spectrophotometric technique they would certainly have discovered any fading and we have assumed therefore that no fading and formation of hydrated salts took place. If in any case (*e. g.*, of low color intensity) there is doubt as to whether sufficient alkali has been added to reach the "end-point" or whether some of the colorless hydrated salt is already present the point can be checked by adding more alkali (ethylate in alcohol) to see whether the color increases or decreases according to theory. This check and the study of fading should be applied most carefully in all cases for short- and long-time periods to correct for the true "end-point" and has been given the closest scrutiny in our own work.[1]

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[1] This is the increase in K_3 observed by introducing the 4 bromines into phenolsulfonphthalein and is used here for illustration. It will be very important to see how K_3 and the other constants are changed by the introduction of the same substituent groups, in the aurine, phenolphthalein, phenolsulfonphthalein and similar series.

[2] This factor omits K'_1H as small in comparison with K_1K_3 in the numerator.

[3] *Am. Chem. J.*, **39**, 534 (1908); **42**, 122 (1909). White and Acree, THIS JOURNAL, **39**, 650 (1917); **40**, 1092 (1918), and forthcoming dissertation. Lubs and Acree, *Ibid.*, **38**, 2773, 2783 (1916).

[4] *Am. Chem. J.*, **18**, 1 (1896); **34**, 441 (1905). Wichelhaus, *Ber.*, **5**, 849 (1872); Posner, *Ann.*, **336**, 85 (1904).

[5] THIS JOURNAL, **33**, 59 (1911). See also Slagle and Acree, *Am. Chem. J.*, **39**, 533, 542 (1908); **42**, 126, 137–9 (1909).

It will be recalled[2] that phenolphthalein ethers, $(C_6H_4COO)C(C_6H_4OR)(C_6H_4OH)$, *p*-oxydiphenyl-phthalid, $(C_6H_4COO)C(C_6H_5)(C_6H_4OH)$, and similar substances dissolve in alkalies as faintly colored or colorless solutions. Green[3] believed that the hydrated salt $KOOCC_6H_4C(OH)(C_6H_4OK)(C_6H_4OR)$ is formed in such cases and one of us has pointed out the evidence[4] on the question whether there may not be a lactoidal salt formed. These are very important cases for the general theory and it is proposed to study the affinity constants of the indicators forming such faintly colored solutions by (*a*) adding the proper indicators to such (nearly) colorless solutions and seeing spectrophotometrically how much indicator salt and colorless salt are formed and hence telling whether the affinity constant of the colorless substance in solution corresponds to the weak phenolic group of the lactoidal form or to a *much stronger* (10^3- to 10^6-fold) carboxyl group of a hydrated form, and by (*b*) using partition between two solvents to measure the hydrolysis and affinity constants to get the same data. It is clear that all of these different phases of the theory must and will be studied in order to get a clear vision of the fundamental underlying causes of these color changes.

Conclusions.

1. Equations are given to show the relation between the specific absorption index (or specific color intensity), or per cent. of intensity colored quinone-phenolate salt, and the equilibrium and affinity constants of the two acid groups of phenolphthalein and phenolsulfonphthalein indicators.

2. A spectrophotometric method is proposed for measuring the concentration of the monobasic yellow quinone phenol salt and of the dibasic intensely colored quinone-phenolate salt in any solution, and the per cent.

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[1] Brightman, Hopfield, Meacham and Acree. THIS JOURNAL, 40, 1940 (1918).

[2] *Ann.*, 354, 171 (1907), *Ber.*, 40, 3728 (1907); *Ibid*, 30, 177 (1897).

[3] Green and King, *J. Chem. Soc.*, 85, 398 (1904); *Ber.*, 40, 3724 (1907).

[4] *Am. Chem. J.*, 39, 532 (1908); 42, 126, 137–9 (1909).

of any indicator transformed into the quinone-phenolate salt in alkaline solution.

3. By the use of the equations and the spectrophotometric data by Howe and Gibson and by ourselves, we have shown that sulfonphthalein indicators are transformed practically completely into quinone-phenolate salts and are therefore very fine, intensely colored indicators. Phenolphthalein is changed to the extent of only about 44% into the intensely colored quinone-phenolate salt, the remainder forming the colorless lactoidal (and hydrated) salts. Tetrachloro-, tetrabromo-, and tetraiodophenolphthalein form only about 1 to 2% of the intensely colored quinone-phenolate salt, the remaining 98 or 99% forming the colorless lactoidal (and hydrated) salts. These indicators are therefore very poor for analytical work. The introduction of 4 chlorines into the phthalic acid residue of phenolphthalein makes phenoltetrachloro-phthalein an excellent indicator which changes to probably 90% or more into the intensely colored quinone-phenolate salt. The introduction of halogens into the phenol groups of phenoltetrachloro-phthalein gives bromo and iodo derivatives, for example, which can give only 17 and 40%, respectively, of the intensely colored quinone-phenolate salt in alkaline solution.

4. We have pointed out how the application of spectrophotometric methods, and the proper equations derived by the use of the mass law, to these indicators gives us for the first time an approximate measure of the real equilibrium and affinity constants of the two acid groups in indicators of the phenolphthalein and the phenolsulfonphthalein types.

5. The disappearance of the violet band at 2300 for phenolsulfonphthalein indicates that in alkaline solution the quinone, or quinone-phenol, group is changed into a quinone-phenolate complex ion like the intensely colored double compounds which Jackson made by the union of quinone and phenolate salts.

SYRACUSE, NEW YORK.

THE LIQUID AMMONIA-SODIUM METHOD FOR HALOGENS IN ORGANIC COMPOUNDS, THE FORMATION OF CYANIDE, AND METHOD OF REMOVING FROM THE SOLUTION.[1]

By Charles William Clifford.

Received March 18, 1919

The literature on the determination of halogens in organic compounds by utilizing metallic sodium or potassium dissolved in liquid ammonia is meager, only two articles[2] being available. Since this method has been known only a comparatively short time and is not widely used, an investigation of its accuracy was undertaken with a view of adopting it in this laboratory.

The Liquid Ammonia-Sodium Method.—The manipulation consists essentially in placing a small quantity of the sample in a Dewar flask and adding liquid ammonia. The material for analysis need not be soluble in the liquid ammonia; if it is insoluble it must be finely divided. Metallic sodium is then added in small pieces until an excess is evidenced by a permanent blue color throughout the solution. By this treatment the halogen of the organic compound is entirely converted into inorganic halide. After evaporation of the excess of ammonia a little alcohol is used to take up any sodium remaining uncombined. The residue is taken up with water and acidified with nitric acid. The halogen is determined usually by precipitation with standard silver nitrate in excess, followed by titration with sodium thiocyanate.

Experimental.

Substances for First Analyses.—Carbon tetrachloride and carbon hexachloride (hexachloro-ethane) were taken as being typical organic compounds although high in halogen. The sample of hexachloride had been recrystallized from alcohol and the tetrachloride was redistilled from c. p. material.

Indications of the Formation of Cyanide.—Analysis of two samples of the tetrachloride sealed in glass bulbs gave an odor upon being acidified, similar to that of hydrocyanic acid, and the following percentages of chlorine were found: 98.40 and 96.80 (theoretical is 92.20).

Proof of Cyanide Formation.—Unweighed samples of both compounds were accordingly treated with sodium in liquid ammonia and qualitative tests for cyanide applied, with these results.

Table I.—Tests for Cyanide.

Method of testing for cyanide.	CCl_4	C_2Cl_6	Blanks.
Ferric ferrocyanide test......	positive	positive	negative
Ferric thiocyanate test	positive	positive	negative

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[1] Published by permission of the Director of Chemical Warfare Service.

[2] E. Chablay, *Ann. chim.*, 9, I, 469–519 (1914); *C. A.*, 8, 3422 (1914); Dains, Vaughan and Janney, This Journal, 40, 936 (1918).

The foregoing results prove the formation of cyanide in these cases. The blanks gave negative tests for halides showing the purity of all reagents in this respect. The formation of cyanide is not mentioned in the references. If formed it must be eliminated or determined in order to arrive at the true halogen content.

Degree of Decomposition of Silver Cyanide and Elimination of Cyanide by Boiling the Nitric Acid Solution.—Some cyanide will be eliminated during the heating of the solution and silver precipitate, as a result of the decomposition of the silver cyanide in the hot dil. nitric acid. Tests using known solutions were carried out to ascertain the completeness of this decomposition and of the elimination of cyanide by boiling in nitric acid solution. Solutions of sodium chloride, sodium bromide, sodium iodide, and sodium cyanide were made up to 0.032 *N* concentration. The chloride was recrystallized from c. p. material by means of hydrogen chloride; the bromide was c. p. material recrystallized once from hot water but was unsatisfactory, possibly due to impurities not removable by this operation; the iodide was c. p. material obtained from a reputable firm. Aliquots of each sodium halide solution equal to 40 cc. of 0.02 *N* were taken and an aliquot of sodium cyanide equal to 38.5 cc. of 0.02 *N* added to each. A definite excess (100 cc. except in two cases) of 0.02 *N* silver nitrate was next added, followed by neutralization with 6 *N* nitric acid, the addition of the specified amounts of 6 *N* nitric acid in excess, and dilution to 250 cc. In the control tests 50 cc. of the silver nitrate was added to the aliquot of the sodium halide before the nitric acid was added. The solutions were then boiled carefully for 3 hours, a much longer heating than in the regular volumetric procedure. The containers were 500 cc. Erlenmeyer flasks covered with watch glasses supported on glass rods. After cooling and filtering, the solutions were titrated with 0.02 *N* sodium thiocyanate, using ferric alum as the indicator. The graduated apparatus had been previously calibrated, and temperature corrections were applied to the solutions; this is true of all quantitative analyses reported in this paper.

TABLE II

Cc of 0.02 *N* Cyanide Undecomposed by Boiling in Dil. Nitric Acid.

	Added 25 cc 0.032 *N*.		
Concentration of acid	NaCl	NaBr	NaI
10 cc. free 6 *N* HNO_3, 250 cc vol . . .	0.07[1] 0.06	0.15	0.24
50 cc. free 6 *N* HNO_3, 250 cc. vol . . .	—0.01[1,2] —0.18[2]	—0.02[2]	0.01[2]

The decomposition of silver cyanide and the elimination of cyanide by oxidation or volatilization by boiling in dil. nitric acid were approximately complete. This is shown by the results, summarized above.

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[1] 50 cc. silver nitrate used.

[2] Solubility of silver halide or volatilization of halogen may possibly affect these.

It is evident, however, that the separation of cyanide and halide is not sharply accurate even with prolonged boiling.

An attempt was made to eliminate the cyanide by boiling the nitric acid solution before the addition of the silver nitrate, and by continuing the boiling until the volume was reduced from 150 cc. to 75 cc. In these experiments actual analyses by the liquid ammonia-sodium method were carried out, the cyanide being that formed in the reaction. Samples of hexachloro-ethane and an aromatic compound containing chlorine and nitrogen were used. The results for the hexachloro-ethane are close to the theoretical, and those for the aromatic compound check results by the sodium peroxide fusion[1] It is possible that minute quantities of cyanide are retained[2] [3] in these analyses, but if so it is in such small amounts that it does not appear in the results. The figures for chlorine were checked by titrating the cyanide[4] in an aliquot with 0.02 *N* silver nitrate (deducting an end-point blank of 0.02 cc.), and subtracting its equivalent from the silver halide plus silver cyanide precipitated in another aliquot of the same sample. As will be seen from the data, the cyanide formed is not a constant for each substance, and is apparently dependent upon factors not ordinarily regulated, in fact, later analyses indicate that in some cases no appreciable amount of cyanide is formed (for example, the analyses referred to by Note 5 under Table VIII, page 1058).

TABLE III

Analysis of Carbon Hexachloride by the Liquid Ammonia-Sodium Method, Eliminating HCN from the Nitric Acid Solution

% cyanide found	% chlorine Calc	% chlorine Found
4.78		89.70
4.35	.	89.87
4.91	89.86	[illegible]
5.11	.	89.66
3.07		89.22
0.87		90.19
		Av., 89.77

That the presence of nitrogen in the compound analyzed is without effect is shown by the following results

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[1] Lemp and Broderson, THIS JOURNAL, 39, 2069 (1917), Parr, *J. Ind. Eng. Chem.*, 11, 230 (1919).

[2] Richards and Singer, *Am. Chem. J.*, 27, 208 (1902); *Am. J. Sci.*, 163, 13, 315 (1902).

[3] Bruckmiller, THIS JOURNAL, 38, 1954 (1916), *Am. J. Sci.*, 192, 42, 498 (1916).

[4] Treadwell-Hall, *Analytical Chemistry*, 1915, II, 711

TABLE IV.

Analysis of Aromatic Compound Containing Chlorine and Nitroge[illegible]

% cyanide found.	% chlorine.		Remarks
	Calc	Found.	
2.92	. . .	40.63 40.71	Tests on 2 blanks gave no cyanide and no halide. Color rendered end-point somewhat difficult to observe. Average of several analyses by sodium peroxide fusion was 40.20% Cl.
6 03	40 76	40.67 40.64	
3 89	. .	40.22 40.3	
		Av., 40.53	

Loss of Halogen in Boiling the Nitric Acid Solution.—Rosanoff and Hill[1] state that in their experiments, boiling 200 cc. of 0.02 *N* potassium chloride after adding 4 cc. of conc. nitric acid, no halogen was found in the distillate of 15 cc., but that when the acid was increased to 6 cc., traces distilled over; with 200 cc. of 0.01 *N* potassium bromide, 3 cc. of the acid caused no loss of bromine, but 3.5 cc. did. Bruckmiller[2] found no loss of chlorine in boiling solutions containing 0.015 g. sodium chloride after adding from 1 to 5 cc. nitric acid in volumes varying from 100 cc. to 25 cc. Lemp and Broderson[2] found no loss of chlorine in boiling the sodium peroxide fusion extract acidified with nitric acid, but demonstrated the probability of inaccurate results in the case of fusions of compounds containing bromine or iodine.

It was desired to check the accuracy of the analyses of organic compounds for chlorine previously given, and to determine whether bromine would be lost in distillation with nitric acid, where an ordinary excess of nitric acid, say 10 cc. of the 6 *N* acid, was used. The following tests were carried out: The solutions of 0 032 *N* sodium chloride, sodium bromide, and sodium cyanide previously described, and 3% halide-free sodium hydroxide were used. Aliquots of the halides equal to 40 cc. of 0.02 *N* were taken and analyzed directly for control, adding first the silver nitrate, then the acid. An aliquot of each halide equal to 40 cc. of 0 02 *N* was then taken, an aliquot of sodium cyanide equal to 38.5 cc. of 0.02 *N* added, then sodium hydroxide equal to 0.8 g. sodium. Each was neutralized with 6 *N* nitric aid and an excess of 10 cc. of the 6 *N* acid added. Each solution was then distilled into 50 cc. of the 3% sodium hydroxide.

The results showed no loss of chlorine, although the boiling was continued until the original volume was reduced from 200 cc. to 100 cc. No chlorine was found in the distillate. However, a small amount of bromine did distil over, due either to oxidation of bromide or volatilization of hydrobromic acid, and here the last portions of cyanide seemed difficult to distil. It is evident from a consideration of these results and those given in the references[1] that all concentrations of reagents must be carefully controlled, if complete and accurate separation of the cyanide and the bromide are to be obtained.

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[1] THIS JOURNAL, 29, 1470 (1907); *C. A.*, 2, 41 (1908).

[2] *Loc. cit.*

Other Separations of Cyanide and Halide.—Since distillation with nitric acid would require very careful regulation of concentrations in order to eliminate practically all cyanide with no loss of chlorine or bromine, and since nitric acid easily oxidizes hydriodic acid, liberating free iodine,[2] a study was made of various other possible methods of separating cyanide quantitatively from the halogens. The following methods were considered:

(*a*) The precipitation of silver cyanide and silver halide together, then making the concentration of nitric acid 10% to 25%, in which silver cyanide is soluble, followed by filtration and titration of the silver cyanide as a *soluble* silver salt.[3] (*b*) Precipitation of silver cyanide and silver halide, followed by separation by the use of mercuric oxide in acetic acid. (*c*) Aspiration of the nitric or acetic acid solution. (*d*) Carbonation of the alkaline solution (*e*) Titration of the cyanide in one aliquot, using silver nitrate, followed by precipitation of both cyanide and halide with silver nitrate in another aliquot This method was tried in several instances, but on account of the multiplication of errors does not give closely agreeing results. This is shown by the following analyses of hexachloro-ethane and an aromatic compound

TABLE V

Determination of Chlorine by Deducting Cyanide from Sum of Cyanide and Chloride.

	Hexachloro-ethane		Aromatic compound containing chlorine and nitrogen	
	Found	Calc	Found	Calc
	89.85		43 54	.
	88.92		0 41	
	91 11	..	40.63	..
	91.83	89 86	40 7	40 76
	90 65		41.84	
	89.89	..	39.6	..
Av.,	90.37		41 13	

(*f*) Precipitation of silver cyanide and silver halide, followed by reduction with zinc and sulfuric acid overnight, filtration, and determination of the halogen. (*g*) Boiling off the cyanide as hydrogen cyanide after acidifying with sulfuric acid[4] (this for chlorides only). (*h*) Distillation of the cyanide as hydrogen cyanide from the acetic acid solution of the halide.[1]

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[1] Rosanoff and Hill, *Loc. cit*; Bruckmiller, *Ibid.*

[2] Lemp and Broderson, *Ibid.*

[3] Gregor, *Z. Anal. Chem.*, 33, 33 (1894)

[4] Richards and Singer, *Loc. cit.*

Method Selected, and Experimental Tests.—The last separation gave promise of being the simplest. Using the previously mentioned solutions of sodium halides, sodium cyanide, and sodium hydroxide, this separation was tested qualitatively and quantitatively.

(1) The purpose of the qualitative tests was to establish the time necessary for the complete elimination of cyanide, with regard to various concentrations of halogen, cyanide, and acetic acid. An aliquot each of sodium chloride and sodium bromide equal to 40 cc. of 0.02 *N* was taken in a 500 cc. Erlenmeyer, an aliquot of cyanide equal to 0.02 g. CN added, then 50 cc. of halide-free sodium hydroxide, which was equal to 0.8 g. of sodium. Each solution was diluted to about 200 cc., neutralized to phenolphthalein with 6 *N* acetic acid, and an excess of about one cc. added. (Preliminary tests had shown that varying the excess of acetic acid from 0.1 to 2.0 cc. had little, if any, effect upon the time of elimination of hydrocyanic acid.) A few clean glass beads were introduced, the Erlenmeyer flask was covered with a watch glass supported on a piece of glass rod, and boiled for $^1/_2$ hour. Each solution was then made slightly alkaline with ammonia, two drops of ammonium sulfide were added, and the solution was evaporated to about 20 cc. The addition of ferric chloride solution proved in each case that cyanide had been completely eliminated.

Tests with higher concentrations of halogen and cyanide were next made in the same manner as just described. The aliquots of halogen were equal to 160 cc. of 0.02 *N*, the cyanide aliquots were equal to 0.08 g. CN, and the sodium hydroxide aliquot was the same as previously. After half an hour's boiling cyanide was still present, so this series was repeated, employing a boiling time of one hour. Tests in this case showed cyanide to be completely eliminated. Aliquots of sodium iodide were not used in these tests, since the addition of ferric chloride would liberate iodine and mask a positive test.

(2) Careful analyses were made to test this method of separation quantitatively. These known solutions were used, and the conditions of the liquid ammonia-sodium method were duplicated as exactly as possible. Two series were run as described under (1). The first contained halogen equal to 40 cc. of 0.02 *N*, cyanide equal to 0.02 g. CN, and sodium hydroxide equal to 0.8 g. sodium, and was boiled for $^1/_2$ hour. The second contained each halogen equal to 160 cc. of 0.02 *N*, cyanide equal to 0.08 g. CN, and sodium hydroxide equal to 0.8 g. sodium, and was boiled one hour. In the case of every solution, after the boiling the halogen was determined by the standard method of precipitation with 0.02 *N* silver nitrate. The solution was then filtered and the excess silver nitrate was titrated with 0.02 *N* sodium thiocyanate. Filtering off silver bromide

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[1] H. E. Williams, "*Chemistry of Cyanogen Compounds*," 1915, 335.

and silver iodide is usually considered unnecessary,[1] but it was done here in order that the end-point might be more accurately observed.

Control determinations were made on an aliquot of each halide after adding an aliquot of sodium hydroxide, for the series of low concentration and the series of high concentration. Half of these were acidified with the acetic acid and boiled, while the remainder were analyzed directly for halogen content. All of these controls agreed within experimental error, showing no mechanical loss by the process of boiling. Duplicate analyses were made in every test described. It was assumed that the acetic radical is without effect in the halogen determination, since silver acetate is much more soluble than silver halide. The results verify this assumption.

TABLE VI

Summary of Analyses of Known Solutions of Sodium Halide, Containing Cyanide.

Halogen content, and variation	NaCl	NaBr	NaI
G. total halogen per cc	0.0011479	0.0025699	0.0039987
G. total halogen per cc. found by experiments	0.0011480	0.0025720	0.0039991
G. halogen per cc. maximum variation in controls	0.0000022	0.0000125	0.0000075
G. halogen per cc. maximum variation in experiments.... .	0.0000012	0.0000130	0.0000084
% maximum difference in experiments .	0.10	0.51	0.21

A consideration of these results shows that in each case the order of accuracy in the experiments was approximately the same as in the controls.

Conclusions from these Test Analyses.—It is proved, then, that the modified liquid ammonia-sodium method is accurate at least within the following ranges:

TABLE VII

Ranges Tested and Found Accurate for the Modified Method

Composition of solution	Lower limit	Upper limit
Volume for boiling . .	175 cc	400 cc.
Halide.	0.002 *N*	0.020 *N*
Cyanide . .	0.05 g. per liter	0.46 g. per liter
Sodium other than sodium halide .	0.0 g.	0.8 g. sodium
6 *N* acetic acid .	0.1 cc	2.0 cc

Analysis of Organic Compounds by the Modified Liquid Ammonia-Sodium Method.

Samples of carbon tetrachloride, hexachloro-ethane, and various organic substances sent into the laboratory for analysis were next analyzed by the modified liquid ammonia-sodium method.

Procedure in Detail.—Samples of liquids of high boiling points were weighed in very thin-walled glass bulbs having short, large, capillary necks. These were introduced into the ammonia and carefully broken with special tongs or by gentle pressure with a heavy glass rod spread at the bottom and having a concave under-surface. If this latter method is used, great care must be taken in order not to fracture the Dewar flask. Unsilvered flasks permit ready observation and allow fairly rapid evaporation. Samples of solids were introduced directly into the flask.

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[1] Rosanoff and Hill, THIS JOURNAL, 29, 273 (1907); *C. A.*, 1, 1367 (1907); *Chem. Zentr.*, 1907, I, 1586.

The sample of 0 05 to 0 25 g. in about 30 cc. of liquid ammonia was treated with an excess of sodium, added slowly in small pieces with frequent stirring, until the blue color persisted 15 minutes. The ammonia was allowed to evaporate. To let stand overnight is convenient, but the time of evaporation may be shortened by blowing dried air from a glass

TABLE VIII.

Summary of Analyses of Organic Compounds by Modified Method

	% halogen			
Compound	Original method	Na_2O_2 fusion	Modified method	Calc.
CCl_4[1]	101 55		93 33	92.20
			93.42	
			Av., 93 37	
C_2Cl_6	89.90[5]		90 37	89 86
			89.74	
			90 23	
			Av, 90 11	
Barium salt of organic sulfonic acid	15 23[5]	15.17	15 02	16 70
		15.05	15 2	
		15.05	.	
		Av., 15.09	Av, 15.13	
Aromatic arsenic-chlorine compound,[2] yellow	13 98[5]	12.80	12.49	12 80
		13 59	13 85	
		13 56	.	
		12.82	...	
		13.15	..	
		Av., 13.18	Av., 13 17	
Aromatic arsenic-chlorine compound, white	14.55	...	13.25	
		13 28	13.33[3]	
		13.32	13.19[3,4]	13 40
		Av., 13.30	Av., 13.26	

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[1] Sample not redistilled.

[2] Compound probably impure, not homogeneous.

[3] Not filtered before precipitating silver halide.

[4] Silver halide not filtered off before titrating.

[5] Little or no cyanide apparently formed.

tube whose outlet is within a few centimeters of the surface. After adding a little alcohol to take care of the excess sodium, water was added, the solution was transferred to a 250 cc. beaker, diluted to about 150 cc., and filtered into a 500 cc. Erlenmeyer flask.[1] This filtration may be dispensed with in many cases. The solution was diluted to 200–250 cc., neutralized to phenolphthalein with 6 *N* acetic acid, and a slight excess (about one cc.) added. A few, clean, glass beads were then added, the flask was covered with a watch glass supported on a piece of glass rod, and boiled carefully at a rather moderate rate for one hour. If more than about 75 cc. of water was vaporized, it was replaced to maintain a fairly constant volume. The solution was cooled somewhat, and the halogen determined by precipitation with silver nitrate, filtration (in most cases), and subsequent titration with sodium thiocyanate.

Method of Titrating to a Definite End-point.—235 cc. of water, 10 cc. of 6 *N* nitric acid, and 5 cc. of 10% ferric alum were taken, and 0.12 cc. of 0.02 *N* sodium thiocyanate added. All determinations were titrated to this same color intensity, using a so-called "Daylight" electric bulb in absence of ordinary sunlight. The sodium thiocyanate was standardized on pure polished silver foil and the silver nitrate by weighing silver chloride, then by checking on the sodium thiocyanate.

Analyses of the last two compounds were completed by the volumetric method, in spite of interfering colors which were intensified by the addition of ferric indicator.

Comparison of this Method, the Carius Method, and the Sodium Peroxide Fusion Method.—This method is much more rapid than the Carius method. As compared with the sodium peroxide fusion, this method possesses the advantage that no blank is necessary, since all reagents can be obtained halide-free without trouble. In the determination of bromine and iodine by this method no oxyacid salts can be formed. The sodium peroxide fusion has been the most widely applicable rapid method for halogens (and sulfur) used in this laboratory. With the liquid ammonia-sodium method side reactions may occur and give rise to interfering compounds and colors, as in the case of aromatic compounds, which make it advisable to decolorize or determine gravimetrically.

Summary.

1. Cyanide is formed in many cases by the treatment of organic compounds with sodium in liquid ammonia. No mention of this is found in the literature.

2. The procedure outlined in the references cannot be followed without involving possibility of error. On acidifying, only a part of the hydrocyanic acid which may have been formed is expelled. At best, the de-

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[1] A thin ring of stopcock grease around the top of the Dewar flask aids in transferring the contents quantitatively to the beaker.

composition of silver cyanide and elimination of cyanide by boiling in dil. nitric acid are only approximately quantitative.

3. The per cent. of cyanide formed is not a constant for each substance, under the conditions of analysis.

4. Treatment with sodium in liquid ammonia completely removes any halogen present in organic compounds. This method is accurate for halogen determination in organic compounds when the resulting halide is separated quantitatively from any cyanide present by acidifying the solution with acetic acid, and then boiling.

5. With chlorine, boiling the nitric acid solution has proved to be a sufficiently accurate elimination of cyanide. An approximate check may be obtained by subtracting cyanide determined in one aliquot from cyanide and halide determined in another aliquot.

The writer wishes to acknowledge his indebtedness to Dr. Albert Finck, under whose supervision this work was performed.

WASHINGTON, D. C.

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF THE GENERAL ELECTRIC CO.]

A METHOD OF GROWING LARGE PERFECT CRYSTALS FROM SOLUTION.

BY R. W. MOORE.

Received March 18, 1919.

In the course of an investigation of some of the electrical properties of crystals, it became necessary to procure large pieces of wholly clear Rochelle salt crystals. It was found impractical to obtain these from commercial sources; a search through tons of crystals yielded only one or two pounds of suitable material. It therefore became necessary to work out some method of producing this material in the laboratory.

During the last few years, considerable work has been done along the line of producing perfect crystals from solution. In 1908, F. Krüger and W. Finke obtained a German patent (German patent 228,246) on an apparatus for the production of homogeneous crystals suitable for physical purposes by crystallizing in motion with a circulating solution. A heating element under delicate control is arranged in a super-saturation vessel and a means for cooling, also under control, between the supersaturation vessel and a crystallizing vessel. In 1915, J. J. Valeton[1] described an improved apparatus based on the above patent.

The growing of crystals by this type of method has apparently been carried to a high state of perfection by J. C. Hostetter,[2] who made various improvements in the details and the construction of the apparatus.

In 1916, the Elektrochemische Werke took out an Austrian patent

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[1] *Ber. Sachs. Ges. Wiss.*, 67, 1–59 (1915).

[2] *J. Wash. Acad. Sci.*, 9, 85–94 (1919).

(Austrian patent 71,587) on an apparatus for growing large crystals from solutions or melts in which the chief novelty was the use of a suction stirrer to produce a lowered temperature and a circulation in the solution.

In 1915, J. M. Blake[1] published an article on the growing of crystals for measurement in which he describes methods of two types. One method consists of cooling a saturated solution slowly. This is accomplished by placing the saturated solution in a bottle, hanging a seed crystal in the solution, suspending the bottle in a cask of warm water packed in sawdust, and allowing the whole to cool down together. Blake states that he had some success with this method and suggests that the bulky cask might be replaced by a smaller reservoir with a source of heat controlled by a thermostat.

The other type of method consists of hanging a seed crystal in a solution of the salt contained in an inclined vessel, suspending a supply of solid salt in the upper end of the vessel, and gently heating this end. Blake states this apparatus can give a steady, constant growth to a crystal and has given good results.

In attempting to grow very large, clear crystals of Rochelle salt, the author first tried the method suggested by Kruger and Finke. Hostetter at this time had not published his article, so that the results of his work were not available. This method gave no successful results, due largely to too crude regulation of the temperature. A cooling method similar to the large cask method used by Blake also gave no satisfactory crystals. Finally, however, a very simple method and apparatus were developed which gave very satisfactory results.

This method consists briefly of placing a small seed crystal or several of them in a nearly saturated solution of the salt, cooling the solution until it is very slightly supersaturated, and maintaining a state of slight supersaturation by slowly cooling the solution, with the temperature regulated within very narrow limits. If the rate of cooling be slow enough, and the temperature does not vary outside very narrow limits, the seed crystals will be build out to form perfectly developed, clear crystals, and will continue to grow clear and perfect as long as the state of slight supersaturation is maintained.

For the production of large crystals of Rochelle salt, our practice is as follows: A saturated solution is made up at some convenient temperature, usually between 35 and 40°. The solution is removed from the excess of salt, heated to a temperature about 7-8° above the saturation temperature, and filtered through paper on a Büchner funnel. The temperature of the solution is not allowed to fall to less than 4-5° above its saturation temperature. Small seed crystals are placed in a jar and the salt solution then poured in. The jar is covered at once with a glass plate and placed in a large water-bath, the temperature of which is about 0.5° above the saturation temperature of the solution. The temperature of the whole is allowed to fall off to practically the saturation temperature as fast as the bath tends to cool. Then, by means of a sensitive thermostat, the rate of cooling is controlled and the temperature allowed to drop at the rate of about 0.1° per day, until the crystals have increased noticeably in size and have built out into perfect crystals. This usually takes only about one day after the saturation temperature is reached. Then the temperature is allowed to fall about 0.2° per day; after the crystals are about $^3/_4$ to 1 inch long, the rate of cooling is increased to 0.3° to 0.4° per day, and when the crystals are well over one inch, to 0.5°–0.6° per day. The thermostat setting is changed twice each day—morning and evening. When the solution has cooled to about room temperature, the jar is removed from the bath and the crystals taken out. They are dried by wiping with a soft, dry cloth.

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[1] *Am. J. Sci.*, 39, 567-570 (1915).

Saturation Curve.—Before a crystallization such as outlined above can be carried out successfully, it is necessary to know exactly at what temperature the solution used will begin to crystallize. In order to determine this factor, we have made careful measurements of the specific gravity of a saturated solution of Rochelle salt at various temperatures over a range from 15 to 39°, and plotted a curve (Fig. 1). From these data, given the specific gravity of a solution that is nearly saturated, the temperature of saturation and hence the temperature at which crystallization will begin is known. Allowance must be made for the fact that the specific gravity is taken (by hydrometer) at a temperature somewhat above the saturation temperature; this allowance proved to be about 0.0005 per degree.

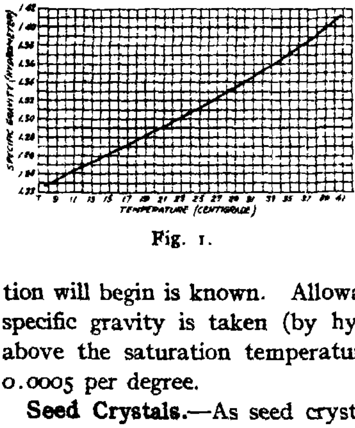

Fig. 1.

Seed Crystals.—As seed crystals, we use small bits of clear crystal about 5 mm. long and 2 mm. thick. In case we have small entire crystals of about the right size, these are used. If not, larger crystals are cut up and pieces are used. In most cases, we have suspended the seed crystals on threads or fine wire. Since there is a tendency for the crystals to dissolve somewhat before the solution cools to the crystallizing temperature, a groove is usually cut around the crystal and the thread or wire fastened around the crystal in the groove. If this is not done, the crystals are very liable to drop out of the loop in the thread or wire. We attempt to choose a crystal of such size that it will not dissolve enough to fall out of the suspension, and yet not larger than necessary. The seed crystal always shows inside the larger crystal and hence we attempt to keep it as small as possible so as to keep as much of the large crystal clear as possible. We have grown a considerable number of crystals lying on glass plates, without any thread in them. The crystals will grow clear under these conditions, but the resulting crystal is not a whole crystal—the side against the glass does not develop. Some few crystals have been grown standing on end on glass plates, but it seems to be much more difficult to get crystals to grow clear and perfect when grown in this position.

In all cases, we have found it desirable to protect the growing crystals from chance crystals, which start spontaneously, by placing in the solution above each crystal or layer of crystals some form of shield, such as a glass plate suspended a few centimeters above the crystals.

The number of crystals grown in a given amount of solution has been varied over a wide range and various forms of containers have been used. The rate at which a crystal grows seems to be the factor which determines whether or not the crystal grows clear and perfect, hence, since the amount of substance which separates out for a definite drop of temperature must be a definite quantity, the rate of growth of any single crystal must depend on the number of crystals in the solution. It should be possible to cool a solution containing several crystals faster than one containing a lesser number and still obtain clear crystals. The relative sizes of the crystals probably also have some effect, and the position in the solution certainly has; the crystals near the bottom of the container grow faster than those near the top. Furthermore, since crystals as they grow larger have a greater area of surface, it should be possible to cool at a more rapid rate when the crystals are large and still have the crystals grow clear. Our results so far have confirmed the above conclusions.

One container which we have used very extensively has been a glass battery jar with a capacity of about 8–10 liters [size about 6 × 8 inches and 12 inches high]. The number of crystals that seems to give the most satisfactory results is about 15, hung in 3 layers and located as far apart as practicable. If more than this number are grown, the crystals are likely to touch and form defective surfaces. A smaller number will give larger crystals, but the rate of growth must be slower.

The other container most used has been a 12-gal. crock, into which 12 gallons of solution has been placed, and in which 36 seed crystals have been suspended. The seed crystals have been hung from frames made of glass rod or heavy nickel wire.

Rate of Growth.—It is not intended that the rate of cooling given in the general outline of the process should be taken as fixed. If there are a considerable number of crystals in one container, the temperature can probably be lowered at a more rapid rate than that given. The temperature changes given are those that will fit most conditions, and are those that we follow at present because they are well within the limits. The maximum rate has not yet been determined; this will, of course, vary considerably with varying conditions.

Water-Baths.—For water-baths we have used various containers. Most of these, however, have been large crocks, usually of 30 gallons capacity. The larger the bath, the more slowly and uniformly the temperature drops. One 100-gallon crock we have used gave very satisfactory results.

The heat is supplied in various ways In one instance we used incandescent lamps immersed in the water with the connections water-tight. In other trials we have had insulated wire heaters immersed in the water, but usually we use a resistance wire wound around the crock and also underneath. All the crocks are covered with heavy felt or asbestos.

Thermostat.—The temperature is controlled by a thermostat, which is sensitive to about 0.01°. This consists of a large glass bulb to which is sealed a capillary tube, resembling a very large thermometer. A platinum wire is sealed through the top of the bulb. To the upper end of the capillary tube is sealed a larger tube, and in this is inserted a rod with a fine screw thread; this screw passes through a threaded cap which rests on the top of the tube. To the bottom of the rod a platinum wire is fastened, and this is inserted into the capillary. The bulb is filled with mercury, which makes contact between the two platinum points at any desired temperature, which temperature can be regulated by the amount of mercury placed in the bulb. The setting of the thermostat can be regulated within very narrow limits by means of the screw.

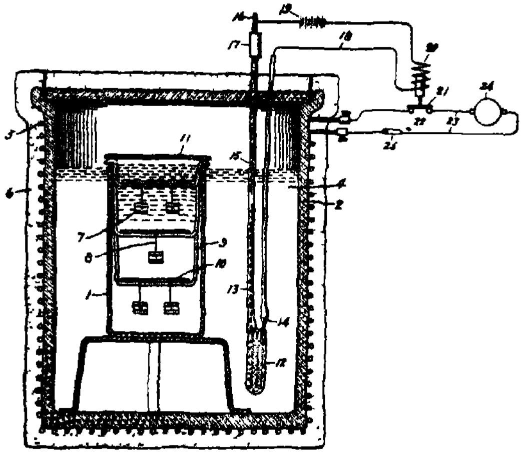

Fig. 2.—1, Glass jar; 2, crock, 4, water, 5, heater winding, 6, felt insulation, 7, seed crystal, 8, thread or wire, 9, glass rod support for 10; 10, 11, glass plates, 12, thermostat bulb, 13, mercury column; 14, 15, platinum wire contacts, 16, screw to the end of which 15 is soldered, and which is carried by threaded cap 17, 18, connections to relay (20, 21, 22) and battery 19, 23, heater connections, 24, generator, source of heating current; 25, switch.

This thermostat is used to operate a relay which opens or closes the heating circuit.

Apparatus.—The arrangement of the whole apparatus in the case where a glass battery jar is used is shown in Fig. 2.

Temperature of Saturation.—The temperature between 32–35° has been chosen as the most practicable. The solution cannot be heated above 55°, since Rochelle salt breaks down at about this temperature. Hence the maximum saturation temperature is about 45°. With the room temperature around 20–22°, it is not easy to work with the solution saturated at 45°, since the temperature of the room is so far below the temperature of the solution that it is difficult to prevent spontaneous crystallization, especially on the surface. The 10–12° range through which we could drop the temperature of the solution has allowed us to grow crystals up to nearly 4 inches in length. In summer, it is desirable to raise the saturation temperature a few degrees.

Washing the Crystals.—We have found considerable difficulty in removing the adhering solution from the finished crystal, without damage to the crystal. Dipping into water even at the same temperature as the solution seems to crack a large proportion of the crystals. Wiping the faces singly with damp cloth or cotton, or drying directly with a dry cloth seem to give the best results, although these methods damage the surfaces and edges slightly.

The beauty of crystals produced by this method must be seen to be appreciated. Beautifully crystallized substances occur abundantly in nature, but the crystals are rarely, if ever, perfectly developed on all faces, due to the fact that the crystals grow with some of their faces in contact with other crystals or substances. By the above method this difficulty is eliminated, and the crystals are given an opportunity of growing perfectly

Fig. 3.

in all directions. The result is a crystal with all angles and faces perfectly formed, thus naturally producing crystals of great perfection and beauty Fig. 3 shows a photograph of a group of Rochelle salt crystals grown by the above method.

Besides Rochelle salt, we have grown crystals of potassium alum, with entire success. Indeed, there seems no reason why the method should not be applicable to many substances which crystallize from solution, either in water or various other solvents, and which have a considerable variation in solubility with change of temperature. Also, it should be possible to grow crystals of two or more isomorphous substances one inside the other. We have succeeded in doing this in the case of potassium and chrome alums, but the resulting crystals were not quite perfect; the manipulation in this case is somewhat more difficult than with a single substance.

It might be noted that growing crystals by this method requires considerable time and patience. In the first place, the saturation temperature of the solution to be used must be carefully determined over at least a small range of temperature around the temperature at which it is proposed to start the crystallization. Furthermore, it will probably require a few trials to determine exactly what temperature ranges are necessary to observe in order that the seed crystals shall not dissolve, and yet spontaneous crystals shall not form. The temperature control apparatus must be in perfect working order, for it must work perfectly over a period of several weeks, without a single miss. If the temperature is allowed to drop too suddenly over even a small range, the crystal does not grow clear, and a cloudy spot or flaw in the crystal is produced. If, by any chance, the temperature rises a little above the saturation temperature, and the crystal dissolves slightly on the surface, and after this the temperature is again lowered, and the crystal grows larger, the outlines of the crystal at the point where it started to grow again always show in the finished crystal. Only when the condition of very slight supersaturation is constantly maintained throughout the growth of the crystal, does the crystal grow perfectly clear. To produce a clear, perfectly developed crystal about 3 inches long has required a period of about one month.

In conclusion, I wish to express my thanks to Mr. F H Guyon and Mr. E. O. Hoffman, who carried out a large portion of the experimental part of this work.

SCHENECTADY, N. Y.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA.]

SOLUBILITY. III. RELATIVE VALUES OF INTERNAL PRESSURES AND THEIR PRACTICAL APPLICATION.

BY JOEL H HILDEBRAND

Received April 11, 1919

1. Introduction.

In the first paper by the writer on this subject,[1] it was shown that deviations from Raoult's law for non-polar substances could be predicted on the basis of differences in internal pressures of cohesions of substances in the liquid state. Since, in systems where it is obeyed, Raoult's law furnishes a method for calculating solubilities of both solids and gases, the prediction of deviations from it makes possible the estimation of relative solubilities. Moreover, we are enabled thereby to understand deviations from a number of fundamental physico-chemical formulas, such as those dealing with molecular weights of dissolved substances, osmotic pressure, Henry's law, the distillation of liquid mixtures, and concentration cells. The wide use to which van't Hoff's law for osmotic pressure is put in deriving physico-chemical formulas emphasizes the importance of an accurate expression for the behavior of substances in solution. The value of Raoult's law in dealing especially with concentrated solutions has begun to be recognized by physical chemists in recent years. Raoult's law is much more accurate at high concentrations than van't Hoff's law and serves quite as well for deriving physico-chemical formulas, in spite of the fact that, as usual in such cases, most text-books in physical chemistry still cling to the historical basis. The present theory, dealing as it does with the deviations from Raoult's law, presents a method of approach to the various problems involving the colligative properties of solutions, concentrated as well as dilute.

In addition to the abundant evidence in support of the theory given in the first paper, still further data were furnished in a second paper on the same subject.[2] It seems safe to say that all of the evidence cited, and this constitutes nearly all at present available, supports the theory that (1) with non-polar substances Raoult's law will be obeyed by mixtures of liquids having equal internal or cohesive pressures, and (2) the greater the difference between the internal pressures the greater will be the escaping tendency of each component of the mixture, and hence the greater the positive deviation of both components from Raoult's law. How this theory could be used to predict solubilities was explained in the first paper, wherein considerable discussion was also included on the effect of polarity.

The most unsatisfactory feature of the previous presentation consisted of the divergent values of the internal pressures, as calculated by other workers, and the uncertainty involved in any attempt to deal with substances other than those given in the table. A study of their methods for calculating internal pressures has shown clearly the necessity for a careful critique of the whole subject. As a preliminary result of this it has been possible to calculate from every simple data by several independent methods the position of each substance in a table of relative internal pressures. The order of arrangement of the substances considered has turned out to be substantially the same irrespective of the method used, so that it becomes possible for one to find very easily the position of a new substance in the table and to answer a variety of questions regarding its solutions.

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[1] THIS JOURNAL, 38, 1452 (1916)

[2] *Ibid.*, 39, 2297 (1917).

No originality is claimed for the fundamental theories used in the following calculations of relative internal pressure, with the exception of the method for relating heat of vaporization to boiling point. A later paper will deal more fully with the theoretical aspects of the problem, this one being designed to present a practical basis for predicting solubilities and for dealing with other problems which may be connected with deviations from Raoult's law.

2. Methods for Calculating Internal Pressure.

(*a*) **Surface Tension.**—It is obvious that work must be done when the surface of a liquid is extended, since a great many molecules are brought from the interior of the liquid, where the attractive forces acting upon a given molecule are the same in all directions, into the surface, where there is an unbalanced attraction towards the interior. This work is numerically equal, on the one hand, to the surface tension, multiplied by the increase in surface. It is equal, on the other hand, to the work done in bringing into the surface against the internal pressure the number of molecules necessary to form the new surface. The work against surface tension is an experimental quantity, and hence would enable us to calculate the internal pressure provided we knew the rate at which this inward attraction decreases as a molecule moves inward from the surface. This idea is contained in the well known equations of Laplace, which require for their integration an assumption as to the law of molecular attraction. Whatever the law expressing the rate of decrease of the unbalanced internal pressure with the distance below the surface, it is very probable that it is a function of the mean molecular distance, which is proportional to the cube root of the molecular volume $V^{1/3}$. Hence we may assume that the work involved in a unit increase is surface, which equals γ, is also proportional to $\gamma/V^{1/3}$. Accordingly, the expression

$$\Pi \propto \gamma/V^{1/3} \qquad (1)$$

should give relative values of internal pressure, at least for liquids whose molecules do not have a very decided orientation in the liquid surface.

A later communication will deal with the values of the proportionality constant resulting from different assumptions for the law of molecular attraction.

(*b*) **Heat of Vaporization.**—Stefan[1] has made the well-known assumption that the work involved in bringing a molecule to the surface of a liquid is $^1/_2$ of that necessary to overcome the entire attraction of the liquid mass involved in vaporization. This leads to the equation

$$\Pi = 20.65 \frac{L - RT}{V}$$

where L is the heat of vaporization. The numerical factor is necessary to convert calories into cc. atmospheres

The writer has shown[2] that there is a very simple relation existing between the vapor pressures of all normal liquids which enables one to calculate the entire vapor pressure curve, and hence the heat of vaporization, from a single point, such as the boiling point. This relation may be used to substitute the more accessible boiling point for the heat of vaporization in making the above calculation By plotting log p against log T for the vapor pressure of one normal liquid a curve is obtained which may be superimposed upon the similar curve for any other normal liquid by sliding it along any line whose equation is $\log p = \log T + \text{const}$. Consequently, when but a single point on the vapor-pressure curve of one substance is known, such as the boiling point, the entire curve may be constructed by the above means Furthermore, the tangent to this curve at any point has a slope equal to L RT From this the value of L at any temperature can be obtained Subtracting RT gives the value of the heat of vaporization at constant volume This was determined for a number of liquids having different boiling points, and it was found that the relation between $L - RT$ at 20° and the boiling point of the liquid could be expressed by the following equation

$$L - RT = 5200 + 30t_b$$

where t_b represents the boiling point.

If Stefan's assumption is correct the internal pressure in atmospheres should accordingly be given by

$$\Pi = 20.65\ (5200 + 30t_b)/V_{20} \qquad (3)$$

Even if the assumption is not absolutely correct it may still represent an approximation sufficient to give relative values of internal pressure for different liquids.

(*c*) **Critical Data.**—As is well known, the term a/V^2 in the van der Waals equation of state represents the internal pressure. If this equation were accurate, values of a calculated from critical data would give true values for internal pressures. Expressing a in the units ordinarily used for van der Waals' equation, the value of internal pressure in atmospheres would be

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[1] Stefan, *Wied Ann*, **29**, 655 (1886)

[2] Hildebrand, THIS JOURNAL, **37**, 970 (1915), **40**, 45 (1918)

$$\Pi = 5.10^8\, a/V^2. \tag{4}$$

Inasmuch as critical data are not available for very many substances, it is gratifying to note that van Laar has contributed a method for the calculation of a on an additive basis.[1] He has shown that $\sqrt{a}$ for a molecule is the sum of the values of $\sqrt{a}$ for the atoms composing it. He gives the following values for $\sqrt{a}\cdot 10^4$:

H	1.6	P	6.4	Kr	6.9
C	3.1; 1.55, 0	S	6.3	Sb	8.9
N	2.9	Cl	5.4	I	8.8
O	2.7	A	5.2	Xe	9.1
F	2.9	Se	7.1	Hg	11
Ne	2.0	Br	6.9		

There is a constitutive influence apparent, especially with carbon compounds, where the surrounding atoms may exert a partial or even complete screening effect. Thus in compounds like CCl_4, C_6H_{14}, and C_2H_5Cl, the value of $\sqrt{a}$ for carbon is 0. In doubly bound carbon, such as in C_6H_6 the value of $\sqrt{a}\cdot 10^4$ is 1.55. It reaches its full value of 3.1 in C_2H_2, CO, etc.

The following examples are reproduced from van Laar's paper:

		$\sqrt{a}\cdot 10^4$.
Cl_2	$(2 \times 5.4)^2$	$= 108$
CS_2	$(3.1 + 2 \times 6.3)^2$	$= 246$
C_6H_{14}	$(0 + 14 \times 1.6)^2$	$= 502$
C_6H_6	$(6 \times 1.55 + 6 \times 1.6)^2$	$= 357$
C_2H_5Cl	$(0 + 5 \times 1.6 + 5.4)^2$	$= 180$
C_4H_4S	$(4 \times 1.55 + 4 \times 1.6 + 6.3)^2$	$= 357$

It is thus possible to calculate values of a with sufficient accuracy for our present purpose of calculating relative internal pressures even where critical data are lacking.

(*d*) **From Coefficients of Expansion and Compressibility.**—From van der Waals' equation we get

$$(\partial p/\partial T)_V = R/(V - b) = (p + a/V^2)/T.$$

Since for liquids p is small compared with a/V^2 we may write

$$(\partial p/\partial T)_V = a/V^2T.$$

We may also write

$$(\partial p/\partial T)_V = -(\partial p/\partial V)_T\,(\partial V/\partial T)_p = \alpha/\beta$$

where α is the coefficient of expansion and β the compressibility. By comparison with the previous expression we get

$$\Pi = a/V^2 = \alpha T/\beta. \tag{5}$$

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[1] *J. chim. phys.*, 14, 3 (1916).

(*e*) **From Coefficient of Expansion.**—Starting again with the van der Waals equation we may differentiate with respect to V, at constant pressure, getting

$$-\frac{2a}{V^3}(V-b)+\frac{a}{V^2} = R(\partial T/\partial V)_p = -\frac{2a}{V^3}\frac{RT}{p+a/V^2}+\frac{a}{V^2}.$$

Neglecting p in comparison with a/V^2 and writing $(\partial V/\partial T)_p = V\alpha$, we have finally

$$\frac{a}{V^2} = \frac{R}{V}\left(\frac{1}{\alpha}+2T\right). \tag{6}$$

The values of R in this equation cannot be evaluated by taking values of α and V at different temperatures, since a/R is constant. We will, therefore, simply take R = 82.1 cc.-atmospheres per degree, giving

$$\Pi = \frac{82.1}{V}\left(\frac{1}{\alpha}+2T\right). \tag{7}$$

A similar expression can be derived for Π in terms of the compressibility, but it is hardly worth while to multiply further expressions derived from van der Waals' equation.

(*f*) **Comparison of Values Obtained by Different Methods.**—On applying the above expressions for internal pressure it is found that very different values are obtained for the same substance. This is illustrated by the values in the following table:

TABLE I.

Internal Pressures at 20°.

	t_b.	$a\cdot10^4$	$\alpha\cdot10^4$.	$\beta\cdot10^6$	V	Π (atmospheres). (3)	(4)	(5).	(6).
Ether . . .	34.6	346	16.5	187.1	103.8	1240	1600	2590	930
Carbon tetrachloride....	76.5	389	12.4	104.5	86.6	1600	2080	3480	1190
Benzene . .	80	373	12.4	95.3	88.8	1770	2360	3810	1300
Carbon disulfide...... .	46	220	12.2	93.2	60.2	2260	3040	3840	1920

The values of β here used are those of Tyrer,[1] the values of a are calculated from the measurements of Young,[2] except that for carbon disulfide, which is from Hannay and Hogarth.[3]

It is not surprising, in view of the well-known inadequacy of the van der Waals equation for dealing with liquids, that the different formulas derived by its aid lead to inconsistent results. It will be profitable in the future to study the results obtained by a similar treatment of other equations of state. Such treatment, however, lies beyond the scope of the present paper, and is unnecessary for the present purpose, since, it will be observed, the values of Π, calculated in the above various ways, are closely parallel (except the value for carbon disulfide, as calculated by

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[1] Tyrer, *J. Chem. Soc*, **105**, 2534 (1914).

[2] Young, *Sc. Proc. Roy. Soc. Dub.*, **12**, 374 (1910).

[3] Hannay and Hogarth, *Proc. Roy. Soc.*, **32**, 294 (1882).

Equation 5, which should be much higher to correspond to the others). Since we are interested primarily in relative and not in absolute values of internal pressure, in order to apply our theory for the deviations from Raoult's law, it suffices to determine the position of a liquid in the table

TABLE II

Relative Internal Pressures at 20°.

Substance	γ	t_b	$a \cdot 10^4$.	V.	$\gamma/V^{1/3}$	$\frac{5200 + 30t_b}{V}$	$\frac{a}{V^2} \cdot 10^4$.
Olein	34.4			994	1.60		
Nickel carbonyl	14.59	43.2	548*	135	2.84	48.0	2.46
Octane	21.52	125	728	177	3.83	50.5	2.32
Decane	22.08	173	968	196.5	3.80	52.8	2.52
Hexane	19.25	69	493	130.5	3.80	55.6	2.90
Ethyl ether	17.1	34.6	346	103.8	3.64	60.1	3.20
Silicon tetrachloride	16.65	59.6		114.5	3.42	61.0	
Mesitylene	28.32	165	684	139.0	5.46	73.0	3.56
Stannic chloride		113	536	117.0	5.44	73.5	3.90
m-Xylene	28.07	139	605	123.0	5.64	76.2	4.00
Ethyl benzene	28.94	136	570	121.0	5.86	76.7	3.90
Carbon tetrachloride	26.56	76.5	389	96.6	5.78	77.5	4.16
Toluene	28.63	110.7	480	106.5	6.06	80.0	4.28
Fluorobenzene	27.96	85	397	93.8	6.18	82.0	4.52
Phosphorus trichloride	29.10	76		87.1	6.07	86.0	
Chlorine		—33.6	118	50.2		84.0	4.60
Benzene	28.90	80	373	88.8	6.48	85.6	4.72
Chloroform	26.76	61	293	80.4	6.20	87.5	4.54
Ethyl iodide	29.08	72	283*	80.7	6.74	91.3	4.35
Chlorobenzene	32.90	132	507	101.8	7.05	90.2	4.88
Bromobenzene	35	156	569	105.0	7.5	94.1	5.16
Naphthalene		218	792	123^1		95.5	5.16
Iodobenzene	37.42	188.5	659	112.2	7.80	96.8	5.24
Ethylene chloride	32.11	83.7	337	78.8	7.50	97.8	5.44
Thiophene	32	84	(413)	79.0	7.5	97.7	(6.62)
			357*				5.72
Phenanthrene		340	1410*	158^2		98.0	5.7
p-Dibromobenzene	39.0	219	860*	120	7.9	98	6.0
Ethylene-bromide	38.36	129	(279)	85.2	8.7	106	(3.9)
			408*				5.5
Phosphoroustribromide		172		95.5		108	
Carbondisulfide	34.5	46	220	60.2	8.7	109	6.1
Bromoform		151	497*	86.6		112	6.6
Sulfurmonochloride	42.95	138	548*	80.5	9.95	116	8.5
Bromine	39	59	191*	51.3	10.5	136	7.3
Iodine		184	310*	60^3		180	8.6
Phosphorus	51.1	287	659	69.5^4	12.4	199	13.7

*Calculated by the method of van Laar, *Loc. cit.*

[1] Extrapolated from data by Lossen and Zander, *Ann.*, **225,** 111 (1884).

[2] Extrapolated from data by Schiff, *Ibid.*, **223,** 247 (1884).

[3] Extrapolated from data by Billet, *Wein. Inst., France*, **1855,** 292.

[4] Abegg-Auerbach, *Handbuch d. anorg. Chem.*, **5,** p. 373.

arranged in the order of increasing internal pressures. This has been done in the preceding table, where, for the sake of simplicity, the numerical coefficients of the formulas have been omitted, also the values calculated by Formulas 5 and 7, since the other values are sufficient and more reliable. Values of $\gamma/V^{1/3}$, Formula 1, have been included, taking the values for γ from the extensive summary by Harkins, Davis and Clark.[1] Values of a and V have in general been calculated from data in *Landolt u. Börnstein Tabellen*, except as noted.

The parallelism between the values in the last 3 columns is quite satisfactory, as it is only occasionally that a difference of more than one or two places is indicated by the different values. In several cases the value of a/V^2 calculated by the method of van Laar corresponds more closely with the position according to other methods than does the one obtained from critical data, which may be considered as evidence of inaccuracy of the latter. It may be remarked that a very decided difference in internal pressure is required to produce any considerable deviation from Raoult's law.

(*g*) **Relative Internal Pressures at —203° C.**—A table similar to Table II may be calculated for the difficultly liquefiable gases, since data are available for some of the more important ones. Table III gives the values obtained for nitrogen, carbon monoxide, argon, and oxygen at —203°.

It was found by the graphic method previously described that the following expression gives the heat of vaporization at constant volume at this temperature:

$$L - RT = -1190 + 26T_b.$$

TABLE III.

Relative Internal Pressure at —203°.

Substance	γ.		$a \cdot 10^4$ [2]	V [3]	$\alpha \cdot 10^6$ [4]	$\gamma/V^{1/3}$	$\frac{L-RT}{V}$	$\frac{a}{V^2} \cdot 10^6$	$\frac{1}{V}\left(\frac{1}{\alpha}+140\right)$.
Nitrogen	10.53	77.3	27	33.35	5600	3.28	24.2	2.43	10.2
Carbon monoxide	12.84	83	28	33.05	4910	4.00	29.4	2.62	10.4
Argon	13.63	87.0° A	26	26.3	4500	4.59	40.7	3.90	13.8
Oxygen	18.35	90.2	27	25.8	3850	6.22	44.6	4.10	15.5

It will be noted that, just as in Table II, there is excellent parallelism between the values in the last four columns obtained by as many independent methods.

3. Use of the Table of Relative Internal Pressures.

(*a*) **Solubility Predictions, Solids.**—The previous papers have discussed the use of the table so far as concerns the substances already in it. The consideration of new substances requires, first, a knowledge of the molecular volume. Where the substance exists in the liquid state this is easily calculated from the molecular weight and the density. When the substance is a gas or a solid at ordinary temperatures its volume as a liquid must be gotten either by extrapolating from its density in the liquid state or by determining its solution volume, preferably in a liquid which would dissolve it obeying Raoult's law. To be very accurate this would, of course, involve one or two successive approximations.

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[1] Harkins, Davis and Clark, THIS JOURNAL, **39**, 541 (1917).

[2] Baly and Donnan, *Trans. Chem. Soc.*, **81**, 907 (1902).

[3] Cf. values in *Landolt-Bornstein Tabellen*.

[4] Calculated from Baly and Donnan, *Loc. cit.*

In addition to the molecular volume of the liquid at 20° we must know also either (*a*) the surface tension at 20°, (*b*) the boiling point, or (*c*) the value of the van der Waals *a*. Where the last is not known from determinations of the critical pressure and temperature it may usually be calculated quite satisfactorily by the method of van Laar explained above.

As examples let us see how successfully we could have predicted the relative solubilities of some of the solids given in the second paper of this series, here reproduced in Table IV.

TABLE IV

Solubilities in terms of mol fraction

Solvent	*p*-Dibromobenzene, 25°	Phenanthrene, 25°	Triphenylmethane, 20°
Hexane	0.086	0.042	0.030
Ether	0.183	0.151	
Carbon tetrachloride	0.193	0.186	
Benzene	0.217	0.207	
Chloroform			0.258
Carbon disulfide	0.224	0.255	0.191
Calc from Raoult's law	0.248	0.221	0.229

Consider first the solubilities of *p*-dibromobenzene. To find the position of this substance in the table, and hence the solvents which would dissolve it giving solutions obeying Raoult's law, we must know its molecular volume in the (supercooled) liquid state, the melting point being 89.3°. Schiff[1] gives an expression for the density of the liquid as follows:

$$d^t = 1.8408 - 0.0009696(t - 89.3) - 0.0002023(t - 89.6)^2.$$

The decimal point in the last coefficient is evidently a misprint, as it leads to absurd results. The coefficient is doubtless either 0.00002023 or 0.000002023, leading to a density at 20° of 1.916 or 1.909, respectively, and a molecular volume of 123 cc. or 124 cc., respectively. Tyrer[2] gives the solution volume per gram at 25° as 0.513 in carbon disulfide, 0.514 in benzene, and 0.506 in chloroform. From these figures we may calculate the molecular volume at 25° to be about 121 cc., which would become about 116 cc. at 20°. We will select 120 cc. as the mean of these two values. The surface tension given in the table is extrapolated from that measured above its melting point. The value of a has been calculated by van Laar's method, which gives $a \cdot 10^4 = (6 \times 1.55 + 4 \times 1.6 + 2 \times 6.9)^2 = 860$. Substituting in our formulas we get values in all 3 cases which agree closely in placing *p*-dibromobenzene close to and a little above carbon disulfide in the table. Its solubility in carbon disulfide should therefore be very close to that calculated from Raoult's law by the aid of the melting point and heat of fusion. Its solubility in liquids higher up in the table should be progressively less. We see that this is the case.

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[1] Schiff, *Ann.*, **223**, 263 (1884).

[2] Tyrer, *J. Chem. Soc.*, **97**, 2620 (1910).

With phenanthrene we have likewise solution volumes from the measurements of Tyrer,[1] from which we may calculate $V = 158$ cc. An expression for the density of the liquid given by Schiff,[2] $1.06305 - 0.0005 (t - 100.5)$, gives a closely agreeing value, 160 cc. Although we do not possess measurements of the surface tension, both the boiling point and the value of a calculated by van Laar's method agree in placing phenanthrene just above *p*-dibromobenzene, so that a similar decrease in solubility is noted as we go to solvents further up the table.

Triphenyl-methane has a molecular solution volume in benzene and in chloroform, according to Tyrer, of 264 cc. at 25°, which we may call approximately 260 cc. at 20°. From this, together with the values $\gamma = 44.7$,[3] $t_b = 360$, $a = 2850 \times 10^{-4}$, (calculated) we calculate the following values: $\gamma/V^{1/3} = 7.1$; $(5200 + 30t_b)/V_{20} = 64$; $a/V^2 \times 10^5 = 4.6$. Although these figures do not agree very closely as to the position of liquid triphenylmethane in the table, they indicate that it belongs in the general region of carbon tetrachloride, benzene and chloroform. As is to be expected from this, we find that its solubility is much greater in chloroform than in carbon disulfide or in hexane.

(*b*) **Solubility Predictions, Liquids.**—It requires a great difference in internal pressures to cause two nonpolar liquids to become incompletely miscible, but the internal pressure of phosphorus is so high that this is possible with all of the liquids at the top of the table. Molten phosphorus forms two liquid phases with carbon tetrachloride and benzene, while with carbon disulfide it is completely miscible at ordinary temperatures. (Molten phosphorus can be greatly supercooled.) It is to be expected that, except as relative internal pressures may be altered by changing temperature, there will be a progressive rise in the critical temperatures of mixing of molten phosphorus with another liquid as we ascend the table. Data upon this are now being obtained.

(*c*) **Solubility of Gases.**—It will be noted that the values expressing relative internal pressures of the gases given in Table III are not far from the values for the liquids at the top of Table II, although Table III is for —203° and Table II is for 20°. Since the internal pressure decreases with the temperature, due to decrease in V, the liquids nitrogen, oxygen, etc., could they exist at 20°, would undoubtedly have very low internal pressures. Hence the substances in Table III properly belong at the top of Table II, and should be much less soluble than corresponds to Raoult's law in all the liquids in Table II, and should, moreover, dissolve most readily in those liquids at the top of Table II. That this is true, so far as existing data are concerned, is seen by reference to the table of gas solubilities given in the first paper of this series

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[1] Tyrer, *J. Chem. Soc.*, 97, 2620 (1910).

[2] Schiff, *Loc. cit.*

[3] Harkins, Davies and Clark, *Ibid.*

It is obvious, further, that the solubility of oxygen should be considerably greater than that of nitrogen in all the solvents in Table II, not only because of its higher boiling point, but also because of its higher internal pressure.

During the war there was some discussion of the possibility of finding a good solvent for carbon monoxide. It is here seen that the best solvents for this gas should be the liquids at the top of Table II, but even in these it should dissolve to a smaller extent than Raoult's law would indicate, and on account of its low boiling point Raoult's law leads us to expect at best but low solubility. The only hope of finding a high solubility would lie in the direction of negative deviation from Raoult's law caused by a solvent with which it would unite reversibly to form a compound in solution.

(*d*) **Distillation of Liquid Mixtures.**—The results obtained in the distillation of liquid mixtures may be related to the partial vapor pressures of the components, and accurately predicted in cases where Raoult's law holds. By adding the possibility of predicting approximately the extent of any deviation from this law we are enabled to get a general idea of what to expect in any case.

Suppose, for example, it were a question of the separation of nitrogen from argon, Table III would lead us to expect a smaller deviation from Raoult's law with this mixture than occurs with mixtures of nitrogen and oxygen, which have been fully investigated.[1]

Again, bromoform and mesitylene, though not differing much in boiling point (151° and 165°, respectively) should give vapor pressures enough greater than Raoult's law, on account of their very different internal pressures, to give a vapor-pressure curve with a maximum, hence a boiling-point curve with a minimum, which would prevent their separation by fractional distillation.

(*e*) **Molecular Weights and "Association."**—In most determinations of molecular weight with nonpolar substances the figures would indicate an increasing association as the concentration of the solute is increased. Investigators have in such cases often used different expressions for concentration in order to make the molecular weight appear as nearly constant as possible. There has been much discussion as to whether the concentration should be expressed in terms of weight of solute per unit volume or per unit weight of solvent, or per unit volume or per unit weight of solution. The question can be decided in the light of the theory that Raoult's law holds for liquids for equal internal pressure Accordingly, in determining molecular weights that solvent should be chosen which will have approximately the same internal pressure and polarity as the solute, and the concentration should be expressed in terms of mol-fraction

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[1] Inglis, *Proc. Phys Soc.*, 20, 640 (1906). Since writing the above the author has discovered measurements of the system argon-nitrogen by Holt and Hamburger (*Z. physik. Chem.*, 91, 513 (1916)) which confirm this prediction.

We may illustrate by using determinations by Beckman of the rise in boiling point of carbon disulfide, using as solutes naphthalene[1] and phosphorus.[2] Table V gives part of the original data, together with values of the mol-fraction of solute N, and the quotient of this into the rise in boiling point, which is the "molecular rise" and can be calculated from the heat of vaporization of the solvent The values of the latter given in the literature are as follows 6670,[3] 6420,[4] 6380,[5] 6600[6] The mean of these is 6520, whence $RT^2/L = 30\ 8$

TABLE V

G CS_2	G solute	Rise in b p Δt	Mol fraction, solute, N	$\Delta t/N$	
				30 8	calculated
49 65	3 746	1 293	0 0438	29 5	solute naphthalene
49 65	6 719	2 268	0 0762	29 8	
54 65	3 129	0 980	0 0339	28 8	solute phosphorus
54 65	6 523	1 810	0 0681	26 6	
49 75	9 349	2 630	0 1032	25 4	

It will be noted that the rise in the boiling point with naphthalene solutions is but slightly less than that calculated from Raoult's law, whereas with phosphorus it is considerably less for similar concentrations. This is exactly what follows from the table of relative internal pressures. Naphthalene and carbon disulfide are not very different in internal pressure, hence the lowering of vapor pressure or the rise in the boiling point of carbon disulfide when naphthalene is dissolved should be a little less than that calculated by the aid of Raoult's law With carbon disulfide and phosphorus, however, the difference in internal pressure is much greater, hence the lowering of vapor pressure or the rise in boiling point is found to be considerably less than Raoult's law would lead us to expect.

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[1] *Z physik Chem*, **6**, 437 (1890)

[2] *Ibid*, **5**, 76 (1890)

[3] Regnault, *Mem Acad*, **26**, 1, 262 (1862)

[4] Winkelmann, *Ann d Physik*, **9**, 208, 358 (1880)

[5] Wirtz, *Ibid*, **40**, 446 (1890)

[6] Andrews, *Pogg Ann*, **75**, 501 (1848)

It is therefore desirable, in determining molecular weights, as well as in determining the "molecular rise," to select solvents having internal pressures approximating those of the solutes. Thus, in the light of the previous discussion concerning the solubilities of *p*-dibromobenzene and triphenyl methane, it is evident that the former would give the normal figure for molecular weight in benzene more closely than in carbon disulfide, whereas with the latter the reverse would be true.

Considerations of this sort may prove very important in such questions as the distinction between S_6 and S_8 for the molecular weight of sulfur, and in work such as that of Gomberg on the trivalent carbon compounds.

It may be well to direct attention to an error easily made in this connection. The vapor pressures of the components of a mixture are related by the Duhem equation $N_1 d\ ln\ p_1 + N_2 d\ ln\ p_2 = 0$, which shows that when the vapor pressure of one component deviates from Raoult's law that of the other will deviate in the same direction. Accordingly, a polar solvent, which we may legitimately regard as associated, will give a smaller boiling or freezing point change with a normal solute than Raoult's law would indicate, causing a high figure, and apparent association, for the molecular weight of the solute. Such a conclusion is, however, quite unjustifiable, since, if the roles of solvent and solute are reversed, the other component would appear to be associated. For example, J. H. Mathews[1] has concluded that anthracene is associated in solution in fused cinnamic acid. Since, however, the latter is a far more polar substance, it, and not the anthracene, is to be regarded as associated, and hence the cause of the deviation from the normal freezing point lowering.

Similarly, Dolezalek[2] has assumed that the deviation from Raoult's law shown by mixtures of benzene and carbon tetrachloride is caused by partial association of carbon tetrachloride. There is, however, more reason to regard the benzene as the slightly associated liquid, so that the assumption is hardly justifiable. The theory here advanced would rather indicate that the difference in internal pressures is responsible for the deviation rather than any difference in polarity. Similar objections apply, of course, to the explanation used by the writer to account for abnormal behavior of various amalgams.[3]

(*f*) **Deviations from the Mass Law.**—Since it is possible to predict when Raoult's law will hold, it is also possible to predict when the mass law will hold for concentrated solutions. The mass law is usually derived for substance in solution by the use of van't Hoff's law for osmotic pressure. This we know to fail at higher concentrations, so that the mass law derived from it must also be inexact. However, derived from Raoult's law, which teaches us to express active mass or concentration in terms of mol-fraction, we can predict that it will hold *at all concentrations* for substances having approximately equal internal pressure, and, moreover, we can predict the direction of the deviation where this is not the case by determining by the aid of differences in internal pressures the relative deviations from Raoult's law.

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[1] Mathews, THIS JOURNAL, 39, 1125 (1917).

[2] Dolezalek, *Z. physik. Chem.*, 64, 727 (1908).

[3] Hildebrand, THIS JOURNAL, 35, 501 (1913); Eastman and Hildebrand, *Ibid.*, 36, 2020 (1914); 37, 2452 (1915).

(*g*) **Partition Coefficients.**—The table enables us to state that in the partition of such a substance as iodine between water and carbon disulfide, there will be for a given concentration in the water layer more iodine in the carbon disulfide than there would be in carbon tetrachloride, in partition between it and water. Illustrations might be multiplied indefinitely.

(*h*) **Recrystallization.**—In purifying substances by crystallizing from hot solution it is desirable to use a solvent in which the substance is not very soluble at ordinary temperatures, but in which its solubility increases as rapidly as possible with the temperature. It is well, also, to choose a solvent in which the impurities which may be present will be as soluble as possible at the lower temperatures. When the substance to be purified has a low melting point it will be very soluble in liquids having a similar internal pressure and polarity, hence it is better to select a solvent different from the solute in one or the other of these factors, so as to produce a smaller solubility. This has the additional advantage of giving a larger temperature coefficient of solubility, for Raoult's law is almost invariably approached more closely at higher temperatures than at lower. For example, a paraffin of melting point below 100° would be most soluble (in terms of mol-fraction) in liquids like hexane, silicon tetrachloride and mesitylene, and its solubility being already a maximum, so far as the choice of solvent is concerned, would not increase so rapidly with temperature as would its solubility in a liquid like carbon disulfide, its solutions with which would deviate considerably from Raoult's law on account of the difference in internal pressure; or in a liquid like alcohol where the deviation would be due to difference in polarity. Hence, in cooling from say 50° to 20°, a greater portion of the paraffin would separate from its solutions in carbon disulfide or alcohol than from a solution in hexane. Moreover, in this case the impurities present would likely be substances of higher internal pressure than the paraffin, such as unsaturated bodies, which would remain in the mother liquor more readily, if the solvent were one of higher internal pressure or polarity.

Where a substance of high melting point, such as anthracene, is being recrystallized, it may be desirable to use a solvent of similar internal pressure in order to secure larger solubility than would be possible in a liquid of very different internal pressure or of high polarity.

In future papers it is planned to discuss the absolute magnitude of internal pressure in the hope of making possible the calculation of the absolute deviation from Raoult's law. Additional solubility data are to be obtained, and the internal pressures of metals are to be examined, so as to make possible the treatment of such quantities as the e. m. f. of amalgam concentration cells, and freezing-point diagrams.

Summary.

Various independent methods for calculating internal pressures of liquids are reviewed, and though the values they yield differ considerably, they are seen to be closely parallel. Pending a theoretical critique of the subject tables of relative internal pressures of relatively nonpolar substances are given for the sake of their practical value.

Other substances may be placed with reference to those already given by knowing their densities (as pure liquids or in solution), together with either surface tension; boiling point; the constant *a* in the van der Waals equation (which may be calculated from critical data or from the atomic values given by van Laar); the coefficient of expansion; or this last, together with the compressibility.

The use of these values is discussed in connection with predictions concerning the solubilities of solids, liquids and gases; the distillation of liquid mixtures; molecular weights and "association," deviations from the mass law; partition coefficients; and the choice of solvent in recrystallization.

BERKELEY, CALIFORNIA

[JOINT CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE UNIVERSITY OF ARIZONA AND NEW HAMPSHIRE COLLEGE.]

THE DETERMINATION OF CERIUM IN THE PRESENCE OF OTHER RARE EARTHS BY PRECIPITATION AS CERIC IODATE.

BY PAUL H. M.-P BRINTON AND C JAMES

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Cerous iodate and the iodates of the other rare earth elements are soluble in the presence of nitric acid, although very difficultly soluble in water. Scandium iodate is soluble in nitric acid, but less easily so than the rare earth iodates. Thorium, zirconium, and ceric iodates are almost insoluble in nitric acid provided a considerable excess of iodate ion be present.

Meyer and Speter[1] have developed a method for the separation of thorium from the rare earth compounds by precipitation as thorium iodate, from a solution strongly acid with nitric acid. It is evident that for the success of this method for thorium any cerium present must be in the trivalent form.

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[1] *Chem. Ztg.*, 34, 306 (1910).

This paper presents the results of an attempt to apply the iodate precipitation to the determination of cerium, and to its separation from the other members of the rare earth group. The hope of success was based on the fact that cerium alone of all the rare earth elements is oxidized to a higher valence by potassium bromate in nitric acid solution.

A solution of cerous nitrate was prepared from material of established purity, which in concentrated state showed no absorption bands when examined by the spectroscope.

A solution of neodymium nitrate was prepared from material of the highest purity. This solution gave no test for cerium when tested with ammonium hydroxide and hydrogen peroxide—an extremely delicate reaction.

A solution of yttrium earth nitrates was prepared from material consisting mainly of yttria, with small amounts of holmia, erbia, and dysprosia. The absence of even traces of cerium compounds in this solution was proved as in the case of the neodymium solution.

These solutions were standardized by precipitation with oxalic acid, and ignition of oxide to constant weight. The concordance obtained in the standardization of the cerous nitrate solutions by 5 portions was within two parts per thousand.

Potassium iodate was used in the form of an acid solution containing 100 g. of iodate and 333 cc. of conc. nitric acid per liter. In some instances the salt was dissolved in the smallest possible amount of dil. nitric acid, and added in this way to prevent undue increase of volume.

The washing solution contained 8 g. of potassium iodate, and 50 cc. of conc. nitric acid per liter.

Potassium bromate was usually added in solid form.

Preliminary experiments indicated that a considerable excess of iodate was necessary to make the precipitation entirely quantitative, and this accords with the experience of Meyer and Speter with thorium. By using about 10 times the theoretical amount of potassium iodate, and maintaining a rather small volume—$^1/_3$ of which was nitric acid—and then adding a little solid potassium bromate, the precipitation of ceric iodate was so complete that the filtrate gave no reaction for cerium by delicate qualitative tests.

The precipitated ceric iodate was first ignited directly, but it was evident that complete conversion to oxide was not to be obtained in this way, as considerable quantities of iodide resulted. Solution of the ceric iodate in hydrochloric acid, with the addition of a little sulfurous acid, and subsequent precipitation as oxalate was found to be feasible, but owing to the presence of mineral acid, which delays and renders less complete the oxalate precipitation, this method was not so successful as the direct treatment of the iodate precipitate with boiling oxalic acid solution. By this direct treatment the precipitate is dissolved, the ceric iodate is reduced, the liberated iodine is expelled, and the cerium is quantitatively precipitated as cerous oxalate.

To test quantitatively the completeness of the precipitation as iodate, and the suitability of the method of direct conversion to oxalate, two samples of the standard cerous nitrate solution were treated with 40 cc. of the precipitating solution. This represented 10 times the theoretical amount of iodate. About 0.5 g. of solid potassium bromate was added to the clear solution, and the resulting precipitate of ceric iodate was flocculated by gently warming. After standing until fully cold and well settled, the precipitate was filtered on a paper of close texture, and washed with the washing solution already mentioned. The precipitate, together with the filter paper, was transferred to the original beaker, 5 g. of oxalic acid and 25 cc. of water were added, and the mixture heated until the paper was well pulped, and all liberated iodine was expelled. 50 cc. of water was added, and after several hours the cerous oxalate was filtered, and ignited to oxide in the regular way, using a platinum crucible over the blast lamp to insure absence of moisture and carbon dioxide in the material to be weighed. The results were ideal, as the following figures, expressed for convenience in grams of CeO_2, will show:

CeO_2· Taken, 0 0721. Found: 0 07 1, 0 0721

The possibility of compensating errors naturally presents itself, and it was regarded as not impossible that a slight solubility of ceric iodate might be compensated by occlusion of potassium salt with the cerous oxalate. The ignited oxides were combined, and repeatedly extracted with boiling water. The residue obtained by evaporating the solution and gently igniting, weighed 0.0003 g., showing that the amount of potassium salt occluded certainly did not exceed 0.00015 g. in each determination. Qualitative tests of the filtrates with comparative color blanks, prepared by taking 0.0002 g. of ceric oxide with ammonium hydroxide and hydrogen peroxide, showed that any cerium present was certainly less than the equivalent of 0.0002 g. of ceric oxide. Thus, if any compensation exists the amounts involved are minute.

The separation of cerium from neodymium was next attempted. By a single precipitation it was found impossible to get a complete separation of cerium and neodymium, and the amounts of cerium found were decidedly too high. By redissolving the ceric iodate, suspended in boiling water, by the gradual addition of nitric acid, as was done with thorium by Meyer and Speter,[1] and then reprecipitating by the addition of more potassium bromate and a very large excess of potassium iodate, the coprecipitated neodymium compound can be entirely eliminated. A series of determinations in the presence of neodymium by the suggested method—working details will be given later—gave promising results.

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[1] *Loc. cit.*

Nd_2O_3 present	CeO_2 taken.	Found.		
0.0475	0.0721	0.0716	0.0721	0.0723
0.1426	0.0721	0.0704	0.0713	
0.2852	0.0721	0.0708	0.0689*	

The results in the presence of the smaller amount of neodymium were satisfactory. With higher percentages of neodymium the results were too low. This was instructive, for in the last 4 determinations of this series it was feared that the results would be too high, and therefore the washing was somewhat extravagantly carried out, and more nitric acid was used in redissolving the first precipitate than was absolutely necessary. The figure marked with an asterisk may have been the result of some manipulative accident, but since none was definitely noted the result is included for the sake of unbiased completeness.

It is evident that the solubility of the ceric iodate is increased by the presence of an unduly large excess of nitric acid, and is decreased by a large excess of iodate ion; so in subsequent experiments the nitric acid was added cautiously until the precipitate just dissolved, and then 15 times the theoretical amount of potassium iodate was added. The washing of the iodate precipitate is best carried out by bringing the precipitate on to the filter paper, allowing it to drain, then rinsing it back into the beaker with the washing solution, and again bringing it upon the filter. The ceric iodate is voluminous, and packs tightly upon the paper. The decantation method of washing is less advisable because if requires a larger volume of wash liquid, in which the precipitate is not absolutely insoluble.

The detailed method as finally adopted may now be given, and then a table of results, together with a discussion of special cases.

To the solution containing the rare earth nitrates (any thorium having been previously removed), is added enough conc. nitric acid so that the latter shall make up $^1/_3$ of the solution. The total solution at this point should not greatly exceed 75 cc. It is also better that the amount of ceria present should not exceed about 0.15 g., since the precipitate is bulky, and the washing is rendered more difficult by the very large precipitate. About 0.5 g., very roughly estimated, of solid potassium bromate is added, and when it has dissolved, an amount of potassium iodate which is 10 to 15 times that theoretically required for the estimated ceria present is added in form of the nitric acid solution already given. This reagent is to be slowly added with constant stirring. The precipitate of ceric iodate is allowed to settle in the cold until the supernatant liquid is practically clear, and it is then filtered on a paper of close texture, such as Whatman No. 42. The precipitate is brought upon the paper pretty completely, and the beaker rinsed just once with a small amount of the washing solution already described. After draining, but not standing longer than is necessary, the precipitate is carefully rinsed from the paper back into the beaker with more of the washing solution. Any clots should be broken up with a stirring rod, and the mixture well churned. The precipitate is again brought on the same filter in the same way, and allowed to drain. It is then rinsed back into the beaker with hot water, heated to boiling, with constant stirring, and conc. nitric acid is dropped in until the precipitate is completely dissolved. Any unnecessary excess of nitric acid is to be avoided. For about 0.1 g. of ceric oxide from 20 to 25 cc. of acid will usually be required. To this solution about 0.25 g. of potassium bromate is added, and about the same amount of potassium iodate as was used in the first precipitation. This may be used in the form of the regular precipitating reagent, unless the use of this solution would make the volume unduly large, in which case the solid potassium iodate can be dissolved by heating in a small volume of 1 : 2 nitric acid, and thus added. The precipitate is allowed to settle as before, and the perfectly cold mixture is then filtered through the original paper, given one very small washing with the nitric acid-iodate washing solution, rinsed back into the beaker once more, well churned, and finally brought on to the paper and washed with 3 small portions of the washing solution. Every trace of the ceric iodate need not be removed from the beaker. The paper with the precipitate is now lifted from the funnel and dropped into the original beaker, taking care to remove any trace of ceric iodate adhering to the glass funnel, either with the upper edge of the filter paper or with a small fragment of another "ashless" filter paper. About 5-8 g. of oxalic acid crystals are now added, and then 50 cc. of water. The covered beaker is heated gently, and its contents are finally boiled until iodine vapors are no longer given off, and all sublimed iodine is vaporized from the cover glass and from the upper edges of the beaker. The cover glass and sides of the beaker are rinsed down with water, and after having stood for several hours the cerous oxalate, mixed with the pulp of the first paper, is filtered, washed with cold water, and ignited in a platinum crucible over the blast lamp. The weight of ceric oxide is obtained by deducting the weight of the two paper ashes.

In the following table are given the results of determinations carried out in the manner just outlined. Any slight deviations from the directions, and interpretations of the effects of these deviations, will be noted later.

In Nos. 1 and 2 the results are somewhat low, and this was attributed to an attempt to economize by using only 4 to 5 times the theoretical amount of potassium iodate, and working in a volume of nearly 200 cc.

In Nos. 15 to 18 the precipitates were rinsed off the paper with hot water, and allowed to stand overnight before attempting to dissolve in nitric acid. It was found impossible to dissolve completely any but No. 17 the next morning, and in all the others a certain amount of the precipitate remained as a sediment. The experiments were repeated in Nos. 19 to 22, under exactly the same conditions, but taking care to dissolve completely the ceric iodate precipitate by the prompt application of nitric acid. The results show that it is necessary to dissolve completely the first precipitate of ceric iodate to free it from admixed rare earth iodates.

No	Nd_2O_3 present G	Y_2O_3, etc., present. G	CeO_2 taken G	CeO_2 found G.
1	0.2852		0.3605	0.3577
2	0.2852		0.3605	0.3575
3			0.0721	0.0719
4			0.0721	0.0717
5			0.0721	0.0718
6			0.0721	0.0722
7	0.1426		0.0721	0.0721
8	0.1426		0.0721	0.0723
9	0.4278		0.0721	0.0722
10	0.4278		0.0721	0.0717
11	0.0475	0.05	0.0721	0.0727
12	0.0475	0.05	0.0721	0.0722
13	0.1426	0.10	0.0721	0.0722
14	0.1426	0.10	0.0721	0.0723
15	0.0475	0.10	0.1442	0.1459
16	0.0475	0.10	0.1442	0.1460
17	0.1426	0.20	0.1442	0.1449
18	0.1426	0.20	0.1442	0.1468
19	0.0475	0.10	0.1442	0.1453
20	0.0475	0.10	0.1442	0.1449
21	0.1426	0.20	0.1442	0.1437
22	0.1426	0.20	0.1442	0.1444
23	0.0950	0.05	0.1442	0.1444

The filtrates from the iodate precipitations will usually show a faint suggestion of opalescence after standing a few days The amount of ceric oxide represented in this is negligible, as the ceric iodate precipitate is voluminous, and even if pure ceric iodate it would contain only about $^1/_6$ of its weight of ceric oxide.

Summary.

A method for the determination of cerium by oxidation with potassium bromate, and precipitation with potassium iodate, followed by direct conversion of the ceric iodate to cerous oxalate has been developed.

This method has been found accurate for determining cerium in the presence of even large amounts of rare earth salts

TUCSON, ARIZ
DURHAM, N H

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF PHYSICAL CHEMISTRY OF THE MASSACHUSETTS INSTITUTE OF TECHNOLOGY, NO. 115.]

THE ACTIVITIES OF THE IONS OF STRONG ELECTROLYTES.

BY DUNCAN A. MACINNES.

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1. The Conductances and Mobilities of the Separate Ions.

Lewis,[1] in his paper on "The Activities of Ions and the Degree of Dissociation of Strong Electrolytes" concludes that hydrochloric acid and the alkali chlorides have the same degree of dissociation at like concentrations. The evidence is based on the following relation:

$$\gamma_1/\gamma_2 = \Lambda_1 n_1/\Lambda_2 n_2 \qquad (1)$$

This expression was derived by R. C. Tolman with the aid of the assumption that the chloride ion has, at any given concentration, the same mobility in solutions of the chlorides of the univalent elements. In this expression Λ_1, Λ_2, γ_1, γ_2, n_1, n_2, denote, respectively, the equivalent conductances, the degrees of dissociation of the two different chlorides, and the transference numbers of the chloride ion in the two solutions. Table I contains data for 0.1 *N* solutions, at 18°, taken from Lewis' article. I have prepared Table II for 0.01 *N* solutions, also at 18°, from data given in Noyes and Falk's[2] compilations. In the sixth column of both tables the product Λn_{Cl} for the several chlorides is divided by the corresponding product for potassium chloride. As this ratio is equal to 1.000 within 0.5%, Lewis concludes that the ionization values are also equal within this limit, although the conductivity ratios, Λ/Λ_0 (given in Col. 3) vary widely, that of hydrochloric acid being about 7% higher than the mean value for the other chlorides. However, in this article mentioned, and in

TABLE I.

Data for 0.1 *N* Solutions of Chlorides.

	$\Lambda_{0.1}$.	$\Lambda_{0.1}/\Lambda_0$	n_{Cl}	$n_{\text{Cl}}\Lambda_{0.01}$	$n_{\text{Cl}}\Lambda/(n_{\text{Cl}}\Lambda)_{\text{KCl}}$
HCl.	351.4	0.925	0.1612	56.7	0.996
KCl.	112.0	0.862	0.508	56.9	1.000
NaCl.	92.0	0.844	0.617	56.8	0.998
LiCl.	82.3	0.833	0.685	56.4	0.992
CsCl	113.4	0.850	0.500	56.7	0.996

TABLE II.

Data for 0.01 *N* Solutions of Chlorides.

	$\Lambda_{0.01}$	$\Lambda_{0.01}/\Lambda_0$.	n_{Cl}	$n_{\text{Cl}}\Lambda_{0.01}$.	$n_{\text{Cl}}\Lambda/(n_{\text{Cl}}\Lambda)_{\text{KCl}}$
HCl	369.3	0.972	0.167	61.67	1.004
KCl.	122.4	0.942	0.502	61.44	1.000
NaCl.	101.98	0.936	0.603	61.44	1.000
LiCl.	91.97	0.931	0.668	61.43	0.9998

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[1] THIS JOURNAL, 34, 1640 (1912).

[2] *Ibid.*, 33, 1436 (1911) and 34, 454 (1912).

a later paper,[1] Lewis decides that the "corrected degree of dissociation" of hydrochloric acid is higher than that of potassium chloride; at 0.1 *N*, for instance, the values given are 81.6 and 78.0, respectively. These "corrected degrees of dissociation" will be discussed in Section 2 of this paper.

The small variation in the values in the last two columns of the two tables shows that the equivalent conductance Λn_{Cl} of the chloride-ion-constituent is, at any given concentration up to 0.1 *N*, substantially the same, whether the other ion-constituent associated with it is hydrogen ion or any of the alkali element ions. This fact makes it very probable that the two factors which determine the equivalent conductance of the chloride-ion-constituent—namely, the degree of ionization γ of the chloride and the equivalent conductance, or mobility, of the chloride ion itself,—must have the same value in the case of the several univalent chlorides at any given concentration, at any rate up to 0.1 *N*, for otherwise we would have to assume that any variation in the value of one of these factors is just balanced by an equal variation of the other factor in the opposite direction. This constancy of the equivalent conductance of the chloride-ion-constituent at any given concentration does not, however, show whether the decrease of it with increasing concentration is due to decrease in the ionization of the chloride, or to decrease in the mobility of the chloride ion, or to simultaneous variation in both these factors. Now, since it is very possible, as already shown, that the ionization is the same in the different chloride solutions, at any given concentration, it is almost certain that the divergence of the conductance ratio Λ/Λ_0 of hydrochloric acid from that of the other chlorides, and the corresponding divergence in the change of the equivalent conductance of the hydrogen-ion-constituent with the concentration from that of the other constituents, are really due to a considerable change with the concentration of the equivalent conductance or mobility of the hydrogen ion itself. And, also, since differences in the variation of the mobilities of the ions are thus demonstrated, it is very probable that actual variations of larger magnitude than these differences occur, with increasing concentrations, in the mobilities of all the ions.

2. The Activities of the Separate Ions.

The preceding considerations, which are based on the kinetic phenomenon of conductance, cannot, from their very nature, lead directly to a determination of the "activity" or "effective concentration" of ions, that is, to a determination of the concentrations which must be assigned to the ions in order that their actual mass action and other thermodynamic effects may be expressed by the familiar laws of perfect solutes. The conclusions reached in the preceding paragraphs do, however, much increase the probability of a simple hypothesis which greatly assists in determining the probable values of the activities of the separate ions. Namely, the fact demonstrated above that the equivalent conductance of the chloride-ion-constituent at a given concentration is independent of the cation constituent, and the strong presumption that the concentration and mobility of the chloride ion is the same at any given concentration in the solutions of univalent chlorides, raises the further presumption that the *activity* of the choride ion, at any given concentration, is also independent of the cation associated with it.

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[1] THIS JOURNAL, 39, 2258 (1917)

This hypothesis differs from that employed, up to the present time, in computing activities. It has been commonly assumed that the cation and anion of the substance have equal activities in the same solution, even in the case of hydrogen ion and chloride ion in hydrochloric acid.

It is the purpose of this section of the article to show how the activities of hydrogen ion can be obtained from existing electromotive force data, with the aid of this hypothesis, and with the further assumption that the usual hypothesis is valid in the case of potassium chloride; that is, that its two ions, which have nearly the same weight and mobility, have the same activity in a solution of the salt.

We will consider cells of the types A and B, *i. e.*, cells without and with liquid junction:

$$\begin{array}{ll} \mathrm{Ag} + \mathrm{AgCl},\ \mathrm{KCl}\ (C_1),\ \mathrm{KHg}_x,\ \mathrm{KCl}\ (C_2),\ \mathrm{AgCl} + \mathrm{Ag}, & \text{(A)} \\ \mathrm{Ag} + \mathrm{AgCl},\ \mathrm{HCl}\ (C_1),\ \mathrm{H}_2\ (1\ \text{atm.}),\ \mathrm{HCl}\ (C_2),\ \mathrm{AgCl} + \mathrm{Ag}, & \end{array}$$

$$\begin{array}{ll} \mathrm{Ag} + \mathrm{AgCl},\ \mathrm{KCl}\ (C_1),\ \mathrm{KCl}\ (C_2),\ \mathrm{AgCl} + \mathrm{Ag}, & \text{(B)} \\ \mathrm{Ag} + \mathrm{AgCl},\ \mathrm{HCl}\ (C_1),\ \mathrm{HCl}\ (C_2),\ \mathrm{AgCl} + \mathrm{Ag}. & \end{array}$$

The electromotive forces E_A and E_B of cells of these two types are given by the following expressions,[1] in which a_1^+, a_1^-, a_2^+ and a_2^- denote, respectively, the activities of the positive and negative ions at the two concentrations C_1 and C_2, and n is the transference number of the cation:

$$E_A = \frac{RT}{F} \log \frac{a_1^+ a_1^-}{a_2^+ a_2^-} \quad \text{and} \quad E_B = \frac{nRT}{F} \log \frac{a_1^+ a_1^-}{a_2^+ a_2^-}.$$

From the electromotive force measurements available for potassium chloride cells of either of these types, by putting $a_1^+ = a_1^-$ and $a_2^+ = a_2^-$, we can find the ratio a_1^-/a_2^- for chloride ion at concentrations C_1 and C_2. Then from the electromotive force data for hydrochloric acid cells, containing acid at the same concentrations C_1 and C_2, we can find, by substituting this value of a_1^-/a_2^- in the appropriate equation, the value of a_1^+/a_2^+ for hydrogen ion.

Table III, which is self-explanatory, contains the available data and the results of the computations just decribed. The electromotive forces in the lines marked J are the measurements of Jahn;[1] in the lines indicated by N. and E. the potentials were interpolated from the work of Noyes and Ellis,[2] by plotting, on a large scale, the logarithms of the observed electromotive forces against the logarithms of the corresponding concentrations. L. B. S. refers to the work of Lewis, Brighton and Sebastian,[3] and M. and P. to that of MacInnes and Parker.[4]

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[1] Lewis, *Proc. Am. Acad.*, 43, 259 (1907) and MacInnes and Parker, THIS JOURNAL, 37, 1445 (1915).

TABLE III.

Substance.	Type of cell.	Temp.	Concentrations. C_1.	C_2.	E. M. F. of cell.	Transference number of cation.	Activity ratios, a_1/a_2 for Cl^-.	H^+.	
HCl.	B	18°	0.006686	0.001665	—0.05614	0.833	3.82	3.84	J.
KCl......	B		0.006700	0.001670	—0.03330	0.495			J.
HCl	B	18°	0.008315	0.001665	—0.06487	0.833	4.70	4.74	J.
KCl......	B		0.008329	0.001670	—0.03844	0.495			J.
HCl......	B	18°	0.01665	0.001665	—0.09235	0.833	8.86	9.38	J.
KCl.....	B		0.01670	0.001674	—0.05434	0.496			J.
HCl......	B	18°	0.03330	0.003329	—0.09162	0.833	8.76	9.14	J.
KCl......	B		0.03347	0.003347	—0.05403	0.496			J.
HCl......	A	25°	0.05	0.005	—0.11234	...	8.64	9.16	N. and E.
KCl.....	A		0.05	0.005	—0.11085	...			M. and P.
HCl......	A	25°	0.1	0.01	—0.1116	...	8.33	9.23	N. and E.
HCl......	A		0.1	0.01	—0.1117	...			L. B. S.
KCl......	A	25°	0.1	0.01	—0.1089	...			M. and P.
KCl........	B		0.1	0.01	—0.0540	0.495			M. and P.

In Table IV the activities of the H^+ and Cl^- ions (Columns 2 and 3) are given at the hydrochloric acid concentrations shown in Col. 1. For the lowest concentration (0.00166 *N*) the activities of the two ions are assumed to be the same and equal to γC, in which γ is the conductance ratio, at this concentration, for potassium chloride. For the activities at 3 of the higher concentrations this figure has been multiplied by the appropriate ratios from Table III. The values corresponding to 0.0033, 0.005 and 0.01 *N* were next obtained by plotting the logarithms of the

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[1] *Z. physik. Chem.*, 33, 545 (1900).

[2] THIS JOURNAL, 39, 2532 (1917).

[3] *Ibid.*, 39, 2245 (1917).

[4] *Ibid.*, 37, 1445 (1915).

TABLE IV.

	Activities.		Activity coefficients.	
Concentrations	K^+ or Cl^-	H^+.	K^+ or Cl^-.	H^+.
0.001665	(0.001627)	(0.001627)	0.976	0.976
0.003330	0.003140	0.003205	0.935	0.972
0.00500	0.004588	0.004750	0.918	0.949
0.00666	0.006215	0.006247	(0.932)	0.937
0.0100	0.008785	0.009257	0.878	0.925
0.01666	0.01441	0.01526	0.864	0.915
0.03333	0.02750	0.02945	0.825	0.883
0.0500	0.0396	0.0434	0.792	0.869
0.100	0.0732	0.0854	0.732	0.854

activities obtained as described above against the logarithms of the corresponding concentrations, the result being very nearly a straight line. These numbers were in turn multiplied by ratios from Table III for the activities at still higher concentrations. Cols. 4 and 5 of Table IV contain the activity coefficients, *i. e.*, the activities divided by the corresponding concentrations. The activity coefficients are based on the same considerations as Lewis' "corrected degrees of dissociations" for salts whose ions have the same activity at any concentration. If the ion activities of a substance are different the "corrected degree of dissociation" is the mean of the activity coefficients.

Since the activity coefficients in Table IV are obtained in part by interpolation and from electromotive force data at two different temperatures, the values given can hardly be final ones. More experimental work is needed in this field. In regard to the temperature, however, the effect on the activity ratios cannot be large since Ellis[1] has found that activity coefficients calculated from freezing-point measurements agree closely with those obtained from electromotive force data at 25°.

3. The Normal Hydrogen *versus* The Normal Calomel Electrode.

Lewis, Brighton and Sebastian[2] have calculated the potential of (hypothetical) molal solution, with respect to hydrogen ion, against the normal calomel electrode. This calculation is repeated below, using the activity coefficients of Table IV instead of the "corrected degrees of dissociations" of these authors.

The potential in question, represented by the expression,[3]

$$H_2,\ H^+\ (M)\ \|\ KCl\ (M),\ HgCl + Hg$$

is the sum of the electromotive forces of the cells:

H_2, HCl (0.1 *M*), HgCl + Hg; $\qquad E = 0.3989$ (C)

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[1] THIS JOURNAL, 38, 761 (1916).

[2] *Loc. cit.*

[3] As in Lewis' papers, the symbol || indicates that correction has been made for the liquid junction.

$\mathrm{Hg + HgCl,\ HCl\ (0.1\ \mathit{M})\ \|\ KCl\ (0.1\ \mathit{M})},$
$\mathrm{HgCl + Hg};\ E = 0.0$ (D)
$\mathrm{Hg + HgCl,\ KCl\ (0.1\ \mathit{M}),\ KCl\ (\mathit{M}),\ HgCl + Hg}\ E = -0.0529$ (E)
$\mathrm{H_2,\ H^+\ (\mathit{M})\ \|\ HCl\ (0.1\ \mathit{M}),\ H_2};\ E = -0.0631$ (F)

Of these (C) is the mean of the closely agreeing results of several observers; (D) is zero, since, according to the viewpoint of this article, the chloride ion has the same activity in both solutions; (E) is a direct measurement of Lewis and Randall; and (F) has been calculated by the usual logarithmic formula using 0.854 from Table IV as the activity coefficient of hydrogen ion in 0.1 M hydrochloric acid. Performing the addition, we obtain

$$\mathrm{H_2,\ H^+\ (\mathit{M})\ \|\ KCl\ (\mathit{M}),\ HgCl + Hg},\quad E = 0.2829.$$

Lewis and his collaborators found practically the same value (0.2828) for this constant.

Following, once more, the method of these authors, this constant can also be calculated by starting from measurements on 0.01 M hydrochloric acid. In this case the potential desired is the sum of the electromotive forces:

$\mathrm{H_2,\ HCl\ (0.01\ \mathit{M}),\ HgCl + Hg},\ E = 0.5105$ (G)
$\mathrm{Hg + HgCl,\ HCl\ (.01\ \mathit{M})\ \|\ KCl\ (0.01\ \mathit{M})},$
$\mathrm{HgCl + Hg}\ E = 0.0$ (H)
$\mathrm{Hg + HgCl,\ KCl\ (0.01\ \mathit{M})\ \|\ KCl\ (0.1\ \mathit{M})},$
$\mathrm{HgCl + Hg},\ E = -0.0545$ (I)
$\mathrm{H_2,\ H^+\ (\mathit{M})\ \|\ HCl\ (0.01\ \mathit{M}),\ H_2}\ E = -0.1203$ (J)

Adding these potentials, together with (E), we obtain

$\mathrm{H_2,\ H^+\ (\mathit{M})\ \|\ KCl\ (\mathit{M}),\ HgCl + Hg},\ E = 0.2828$

agreeing exactly with the above workers. Potential (G) is from the article quoted; (H) is based on the same assumption as (D); and (I) and (J) were found by using activity coefficients from Table IV. Although, in this case, the same result is obtained as that found with the usual assumptions as to activities, some of the potentials making up the totals have quite different values. For instance, the article quoted gives 0.0012 for (D), the potential arising from the supposed difference in the activities of the chloride ions in the two solutions.

An example of the difference between the proposed system and the usual assumptions appears in the computation of the liquid junction

$$\mathrm{HCl\ (\mathit{C}_1),\ HCl\ (\mathit{C}_2)}.$$

If the concentrations are, for instance, 0.01665 and 0.001665 N, the assumption of equal activities of the two ions leads to —0.03694 for the potential at this point of contact,[1] whereas the activity values given in

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[1] This Journal, 37, 2305 (1915).

Table IV yield —0.03767. The latter figure also gives the same potential (0.05468) for the systems:

Ag + AgCl, HCl (0.01665) || HCl (0.001665), AgCl + Ag

and

Ag + AgCl, KCl (0.01665) || KCl (0 001665), AgCl + Ag

as would be expected if hydrochloric acid and potassium chloride are equally dissociated, since all the electrodes are reversible to the chloride ion. These computations will be discussed further in a forthcoming article.

I am indebted to Prof. A. A. Noyes for valuable criticism in the preparation of this paper.

4. Summary.

Since the product of the transference number of the chloride ion and the equivalent conductance $n\Lambda$ is a constant, at a given concentration and temperature, for the chlorides of the alkali metals and of hydrogen, it has been assumed that the "activity" of the chloride ion in these solutions is also independent of the nature of the (univalent) positive ion. On this basis the activity coefficients of both ions of hydrochloric acid have been calculated for a series of concentrations, and the potential of the normal hydrogen electrode against the normal calomel electrode has been computed.

CAMBRIDGE, MASS

NOTE.

Corrections.—In the paper entitled "Notes on Neutral Salt Catalysis" (THIS JOURNAL, 40, 1461 (1918)). On p. 1463, Equation 2 should read $H_2O_2 + IO' = H_2O + I' + O_2$, instead of $H_2O_2 + IO' = H_2O + IO'_2$; on p. 1477, in the middle of the page, for $E_l + E_t$ read $E_t - E_l$; in the last line, for $E_t + E_l$ read $E_t - E_l$; on p. 1478, in Table VII, all numbers in the column headed E_l should be positive instead of negative; the column headed $E_t + E_l$ should read $E_t - E_l$; and on p. 1479, in Table VIII, under the column headed $\frac{K \times 10^2}{a_1}$, read 14 14 for 13.14.

HERBERT S. HARNED

JOHN HARRISON LABORATORY,
UNIVERSITY OF PENNSYLVANIA,
PHILADELPHIA.

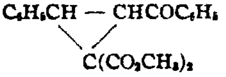
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY.]

STUDIES IN THE CYCLOPROPANE SERIES. V.

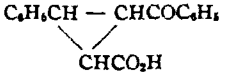
BY E. P. KOHLER AND L. L. STEELE.

Received March 12, 1919

All the cyclopropane derivatives described in the earlier papers had two carboxyl groups in combination with one of the carbon atoms of the ring. In order to determine to what extent the peculiar properties of those substances are due to this fact we have studied derivatives which differ from them only in having hydrogen in place of one of the carboxyl groups. The relation between the two types is shown by the formulas

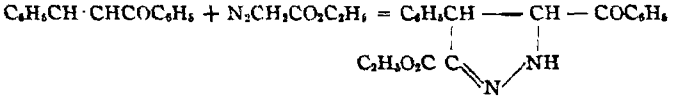


(I).

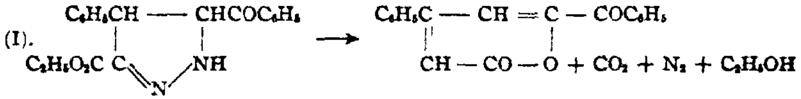


(II).

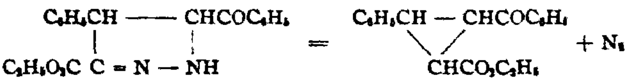
The preparation of cyclopropane derivatives of the general type represented by Formula II proved exceedingly difficult; but was finally accomplished by an adaptation of the pyrazoline method used by Buchner for preparing cyclopropane acids. Under suitable conditions, α,β-unsaturated ketones combine with ethyl diazo-acetate to form pyrazoline derivatives:



These ketonic pyrazolines decompose when heated but unlike the corresponding esters give, almost exclusively, pyrone derivatives:

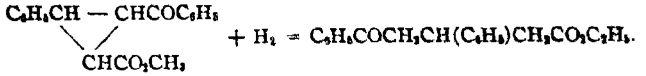


A small quantity of cyclopropane derivative is, however, formed in accordance with the equation

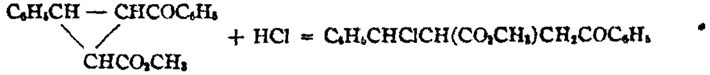


The yield of cyclopropane ester is less than 1% but we found that by heating the pyrazoline in contact with polished platinum it was possible to speed up the second reaction at the expense of the first and thus increase the yield to more than 40%. The pyrone derivatives, which always constitute the main product, are not due to a decomposition of the cyclopropane compounds at high temperatures because these are far more stable than the corresponding substances of Type I, and can be heated without change to temperatures more than 100° above those used for decomposing the pyrazolines.

We have studied the behavior of our substances with all the reagents that give characteristic results with the cyclopropane derivatives of Type I: oxidizing agents, reducing agents, halogen acids, halogens, phosphorus pentachloride and alcoholates. Toward oxidizing agents they present the same contrast with ethylenic compounds that was noted in the earlier work, being quite unaffected by permanganate but readily reduced by zinc and acetic acid. Reduction results in addition of hydrogen to the ring carbon atoms, (1) and (3), and the product is a saturated δ-ketonic ester.



Both the acids and their esters combine with halogen acids at least as readily as do α,β-unsaturated ketones, the ring opening between carbon atoms (2) and (3).

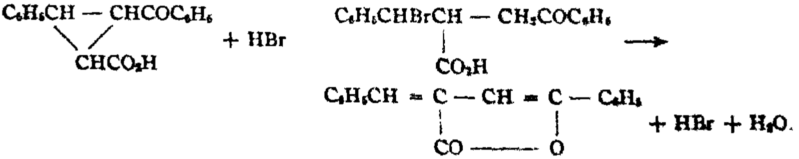


The resulting chloro ester loses hydrogen chloride to potassium acetate with the greatest ease, and it is noteworthy that while it is a β-chloro ester as well as a γ-chloro ketone, not a trace of unsaturated ester is formed in the process, the sole product being the cyclopropane derivative. The corresponding chloro acid, however, behaves toward sodium carbonate like a typical β-halogen acid, giving β-benzal-propiophenone.[1]

$$C_6H_5CHClCH(CO_2Na)CH_2COC_6H_5 = C_6H_5CH = CHCH_2COC_6H_5 + HCl.$$

The reactions with halogen acids and reducing agents in which the ring is opened in different positions constitute the real proof that these substances are cyclopropane derivatives and not isomeric unsaturated δ-ketonic acids.

Dehydrating agents like acetic acid and acetic anhydride by themselves do not have any effect on the cyclopropane derivatives but in their presence hydrogen bromide rapidly transforms the cyclopropane acids into unsaturated lactones.



Thionyl chloride and phosphorus pentachloride convert the cyclopropane acid into its chloride without attacking the ring. The acid chloride cannot, however, be used for the preparation of ketones by the Friedel and Crafts reaction because when it is treated with benzene and aluminum chloride it immediately passes into the unsaturated lactone. This is probably merely another illustration of the action of the halogen acids in the presence of dehydrating agents.

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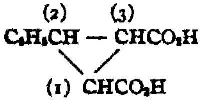
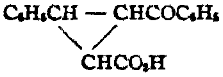
[1] Wieland, *Ber.*, 40, 4830 (1907).

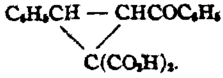
A comparison of 3 closely related types of cyclopropane derivatives shows some significant differences.



(I).



(II).



(III).

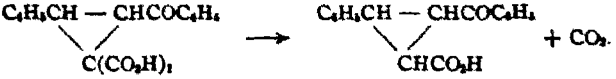
Buchner found that the acids of Type I as well as their esters are perfectly stable at high temperatures, and also that the cyclopropane ring in these substances can not be opened with reagents. We have verified this; both the acids and their esters behave in every respect like saturated compounds. In contrast with this, the other two types of substances give many of the addition reactions of unsaturated compounds.

The most conspicuous difference between the substances represented by II and III is in their behavior towards basic reagents. The esters of the dibasic acids combine with the greatest ease with alcoholates, sodium amide, and similar substances, the ring opening between carbon atoms (1) and (3). In contrast with this the esters of the monobasic acid are indifferent to dry alcoholates, and no reagents were found which would open the ring at this point. Both types combine with hydrogen, the halogen acids, and probably the halogens.

The *mode* of addition to substances of Types II and III is the same in all cases in which they combine with the same reagents. The *ease* of addition, however, is quite different. The acids of Type III pass into lactones, essentially an addition reaction, at temperatures at which those of Type II are perfectly stable. With halogen acids, on the other hand, the substances of Type II combine far more readily than those of Type III.

Experimental Part.

Preparation of the Cyclopropane Derivatives.—When benzoylphenylcyclopropane dicarboxylic acid is heated, one of the products is the corresponding monobasic acid.[1]



The amount of cyclopropane derivative obtained in this way is insignificant but it seemed probable that by using ester acids, acid salts, or suitable catalytic agents, it would be possible to lower the temperature to the point where the cyclopropane derivative would be the principal product. All of our efforts in this direction proved fruitless.

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[1] This Journal, 39, 1418 (1917).

The second method of preparation that we tried depended on the elimination of hydrobromic acid from an α-bromo ketonic ester. For the work in this direction we selected methyl β-phenyl-γ-(4-bromobenzoyl)-butyrate, because it was more likely to give solid products than the unsubstituted ester.

β-Phenyl-γ(4-bromobenzoyl)-butyric Acid, $BrC_6H_4COCH_2CH(C_6H_5)CH_2CO_2H$.—The acid was obtained in calculated quantity by heating the corresponding malonic acid[1] to 135–140° until effervescence ceased. It was purified by recrystallization from aqueous alcohol. It separated in needles and melted at 152–153°.

Calc. for $C_{17}H_{15}O_3Br$: C, 58.8; H, 4.3. Found: C, 58.5; H, 4.5.

The methyl ester was obtained by saturating a concentrated solution of the acid in methyl alcohol with hydrochloric acid. It separated in solid form as the solution cooled. The solid was washed with water and recrystallized from methyl alcohol. The ester crystallizes in stout needles, is moderately soluble in methyl alcohol and ether, and melts at 93°.

Calc. for $C_{18}H_{17}O_3Br$: C, 49.1; H, 3.6. Found: C, 48.9; H, 3.6.

Methyl β-Phenyl-γ-bromo-γ-(4-bromobenzoyl)-butyrate, $BrC_6H_4COCHBrCH(C_6H_5)CH_2CO_2CH_3$.—The ester was brominated in carbon tetrachloride. The product was left as an oil when the solvent was removed under diminished pressure, but it solidified on addition of a little ether. By recrystallization from methyl alcohol the solid was separated into two monobromo derivatives. The one that is formed in largest quantity crystallized in fine needles and melted at 81–82°. The other separated in small quantity from the mother liquors, in long, feathery crystals that melted at 92°.

Calc. for $C_{18}H_{16}O_3Br_2$: C, 49.1; H, 3.6. Found: C, 49.0, 49.1; H, 3.6, 3.9.

Elimination of Hydrogen Bromide.—Methyl alcoholic solutions of the γ-bromo esters were boiled with magnesium methylate, potassium acetate, and sodium methylate. The substance was not affected at all by magnesium methylate. The solutions containing potassium acetate deposited nearly the calculated amount of potassium bromide in the course of 5 hours. Most of the alcohol was then removed. It left a pale yellow oil. This was dissolved in ether, the ethereal solution washed, dried and allowed to evaporate. The pale yellow oil that was left eventually solidified. The solid was purified by recrystallization from alcohol and thus obtained in fine, colorless needles that melted at 158°.

Calc. for $C_{17}H_{13}O_3Br$: C, 59.1; H, 3.8. Found: C, 58.8; H, 3.4.

The analysis indicated a lactone, formed in accordance with the equation

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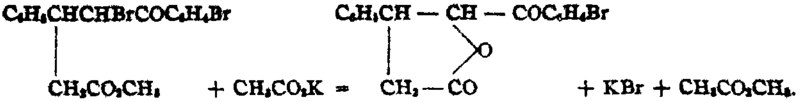
[1] THIS JOURNAL, 39, 2408 (1917).



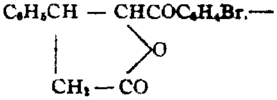
$$\begin{array}{l} C_6H_5CHCHBrCOC_6H_4Br \\ | \\ CH_2CO_2CH_3 \end{array} + CH_3CO_2K = \begin{array}{l} C_6H_5CH - CH - COC_6H_4Br \\ |\qquad\quad > O \\ CH_2 - CO \end{array} + KBr + CH_3CO_2CH_3.$$

In order to verify this the γ-lactone was made by way of the bromo acid.

β-Phenyl-γ-bromo-γ-(4-bromobenzoyl)-butyric Acid, $BrC_6H_4COCH-BrCH(C_6H_5)CH_2CO_2H$.—Bromine was added to finely powdered phenyl-*p*-bromobenzoyl-butyric acid, suspended in hot carbon tetrachloride, until a permanent red color appeared. The acid dissolved in the process and the solution on cooling deposited the bromo ester in calculated quantity. The fine, white powder was recrystallized from ethyl acetate, as it was found to be excessively soluble in alcohol and ether. It crystallized in needles and melted at 146–147°.

Calc. for $C_{17}H_{14}O_3Br_2$: C, 47.9; H, 3.3. Found: C, 47.8; H, 3.1.

β-Phenyl-γ-(4-bromobenzoyl)-butyrolactone,

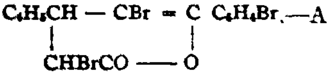


$$\begin{array}{l} C_6H_5CH - CHCOC_6H_4Br \\ |\qquad\quad > O \\ CH_2 - CO \end{array}$$

—The γ-bromo acid was dissolved in a cold solution of sodium carbonate. After 3 or 4 minutes the clear solution became turbid and soon a precipitate formed. This was recrystallized from alcohol and a mixed melting point showed that it was identical with the product obtained from the reaction between the bromo ester and potassium acetate.

The product of the reaction between the bromo ester and sodium methylate likewise was an oil that solidified after long standing. The solid proved to be a mixture of the same lactone and the bromine-free saturated ester in approximately equal amounts. These results showed that it was hopeless to attempt to get the cyclopropane derivative from the γ-bromo ester.

3,5-Dibromo-4-phenyl-6-(4-bromo-phenyl)-dehydropyrone-1,2,

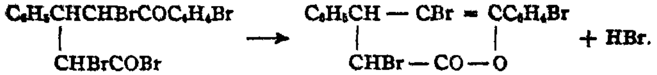


$$\begin{array}{l} C_6H_5CH - CBr = C\ C_6H_4Br \\ |\qquad\qquad\qquad | \\ CHBrCO - O \end{array}$$

—A third attempt to make the cyclopropane derivative was based on the elimination of bromine from an α,γ-dibromo ketonic ester As the γ-bromo ester does not react with bromine we undertook the bromination of the γ-bromo acid by the Hell-Volhard-Zelinsky method. For this purpose 5 g. of the acid was dissolved in 12 g. of phosphorus tribromide with gentle warming. An excess of bromine was added and the mixture boiled until the evolution of hydrogen bromide ceased. The solution was then allowed to cool and poured into ice water. This precipitated a brick-red solid which was insoluble in alcohol and ether. It was recrystallized from ethyl acetate from which it separated in large, rhombic crystals of the color of smoky quartz. These melted at 170°.

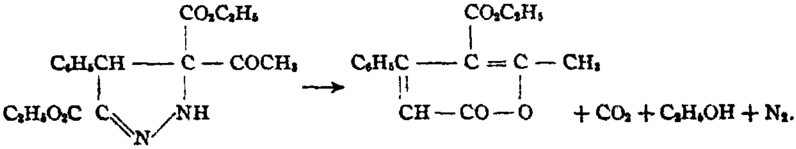
Calc. for $C_{17}H_{11}O_2Br_3$: Br, 49.3. Found: 49.4.

The substance was insoluble in alkaline carbonates. No attempt was made to determine its structure, but it seems altogether probable that it is a pyrone derivative formed from the acid bromide.



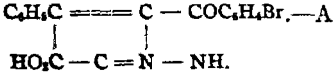
$$\begin{array}{l} C_6H_5CHCHBrCOC_6H_4Br \\ | \\ CHBrCOBr \end{array} \longrightarrow \begin{array}{l} C_6H_5CH - CBr = CC_6H_4Br \\ | \qquad\qquad\qquad | \\ CHBr - CO - O \end{array} + HBr.$$

Ketonic Pyrazolines.—Since all of the more direct methods for getting the desired cyclopropane derivatives failed it became necessary to resort to the pyrazoline reaction which Buchner used for making cyclopropane acids. The outlook was far from promising. Ketonic pyrazolines are not nearly so easy to make as the pyrazoline esters; and only few are known.[1] Most of these were made by Buchner for the purpose of getting cyclopropane derivatives, but when he heated them he invariably obtained only pyrone derivatives.[2]



The diazo ester used in the earlier experiments was a very pure preparation obtained by the method of Curtius.[3] It was found later that a product obtained by the more convenient method given by Weyl[4] served equally well. After removing the last of the ether under diminished pressure the pale yellow liquid could be kept in brown bottles for many weeks without change. In a colorless bottle one specimen polymerized to the triethyl ester of pyrazoline triacid-1,2,3, melting at 98–99°.

Phenyl-(4-bromobenzoyl)-pyrazole Carboxylic Acid,



$$\begin{array}{l} C_6H_5C = C - COC_6H_4Br. \\ | \qquad\quad | \\ HO_2C - C = N - NH. \end{array}$$

—A mixture of equivalent amounts of ethyl diazo-acetate and benzal-*p*-bromo-acetophenone was warmed gently on a steam-bath. At 90° a slight effervescence was noted and at 95° a vigorous reaction took place. After this was over the temperature of the mixture was gradually raised to 175° in the course of 4 hours. The product on cooling turned to a glue-like mass which did not solidify in contact with alcohol. It was, therefore, treated with alcoholic potassium hydroxide. The solid potassium salt which separated was washed with alcohol until colorless. It gave a colorless acid which crystallized from alcohol in feathery needles. The acid melted, with decomposition, at 216–217°.

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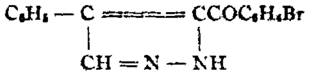
[1] *Ber.*, **28**, 221 (1895); **35**, 34, 785 (1902).

[2] *Ber.*, **35**, 789 (1902).

[3] *J. prakt. Chem.*, [2] **38**, 401 (1888).

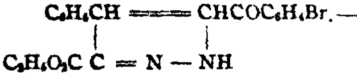
[4] *Meth. d. org. Chem.*, p. 848.

Calc. for $C_{17}H_{13}O_3N_2Br$: Br, 21.6. Found. Br, 21.2.

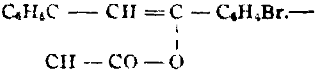
Phenyl-(4-bromobenzoyl)-pyrazol, 
$$\begin{array}{lcl} C_6H_5-C & = & CCOC_6H_4Br \\ | & & | \\ CH=N & - & NH \end{array}$$
—The pyrazol carboxylic acid began to effervesce freely at 245°. The gas evolved was carbon dioxide. The light brown residue was recrystallized from alcohol, which deposited it in colorless needles melting at 159°.

An analysis of this substance showed that it was a pyrazol derivative; the condensation product from which it was obtained therefore was not the desired ketonic pyrazoline

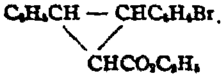
Calc. for $C_{16}H_{11}ON_2Br$ C, 58.7; H, 3.4. Found C, 58.7, H, 3.7

Ethyl 4-Phenyl-5-(4-bromobenzoyl)-pyrazoline Carboxylate, 
$$\begin{array}{lcl} C_6H_5CH & = & CHCOC_6H_4Br \\ | & & | \\ C_2H_5O_2C\,C=N & - & NH \end{array}$$
—A solution of 15 g of ethyl-diazo-acetate and 37 g. benzal-*p*-bromo-acetophenone in high boiling ligroin was heated on a steam-bath. After a time a fine, white precipitate began to separate. The reaction appeared to be complete after 2.5 hours when 26.5 g. of product was filtered from the hot solution. Recrystallization of this product from alcohol gave colorless, rhombic plates which melted at 150–154° with effervescence.

Calc for $C_{19}H_{17}O_3N_2Br$ C, 56.8, H, 4.2 Found C, 56.9, H, 4.5

4-Phenyl-6-(4-bromophenyl)-pyrone-1,2, 
$$\begin{array}{l} C_6H_5C - CH = C - C_6H_4Br \\ | \\ CH - CO - O \end{array}$$
—The pyrazoline derivative began to give off nitrogen at 160°. A quantity of it was therefore heated in an oil bath at 170-200° for two hours. The resulting oil on cooling deposited a mixture of two kinds of crystals. These were separated by systematic fractional crystallization from alcohol. The principal product was sparingly soluble in alcohol from which it separated in fine, feathery crystals When pure it melted sharply at 183° and contained no nitrogen This was evidently a pyrone derivative formed in the same way as those obtained by Buchner in a similar reaction.

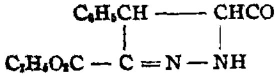
Calc. for $C_{17}H_{11}O_2Br$ C, 62.4, H, 3.4 Found C, 62.2, H, 3.6

Ethyl 2-Phenyl-3-(4-bromophenyl)-cyclopropane Carboxylate, 
$$\begin{array}{c} C_6H_5CH - CHC_6H_4Br \\ \diagdown\ \diagup \\ CHCO_2C_2H_5 \end{array}$$
—The mother liquors from the pyrone derivative deposited a small quantity of another substance. By recrystallization from alcohol this was obtained in colorless needles which melted at 118–119°.

Calc. for $C_{18}H_{17}O_2Br$: C, 61.1; H, 4.6. Found C, 61.0, H, 4.4.

This substance was undoubtedly the cyclopropane derivative, but the amount obtained was extremely small—less than 0.1 g. from 10 g. of pyrazoline derivative. Its relatively high melting point and its sparing solubility in alcohol indicated that a corresponding compound obtained by starting with benzal-acetophenone would likewise be a crystalline solid. We therefore used the more convenient unsaturated ketone in all subsequent experiments.

Ethyl 4-Phenyl-5-benzoyl-pyrazoline Carboxylate-3,



$$\begin{array}{l} C_6H_5CH \text{ ——— } CHCOC_6H_5 \\ \quad\ \ | \qquad\qquad\ | \\ C_2H_5O_2C - C = N - NH \end{array}$$

.—A solution of 43.8 g. of benzal-acetophenone and 24 g. of ethyl diazo-acetate in the minimum quantity of ligroin (90–120°) was heated on a steam-bath for 3 hours. A red oil accumulated on the bottom and sides of the flask. The ligroin was decanted and a small quantity of ether poured on top of the oil, which soon solidified under this treatment. The solid, purified by recrystallization from alcohol, was obtained in hexagonal plates melting at 156–158°.

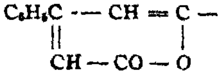
Calc. for $C_{19}H_{18}O_4N_2$: C, 70.8; H, 5.6. Found: C, 70.5; H, 5.9.

In later experiments it was found that a much purer product could be obtained by inoculating the hot ligroin solution of benzal-acetophenone and ethyl diazo-acetate with some of the crystalline pyrazoline derivative and then by frequent shaking induce the product to separate as a fine crystal powder. After this was washed with ether it was pure enough for use. It was found also that on a small scale, at any rate, the reaction can be carried out without using a solvent. Thus 2 g. of unsaturated ketone and 1.2 g. of the diazo compound were heated at 60–65° for 5 hours. The pyrazoline derivative began to separate spontaneously after about an hour. After washing with ether the product weighed 2. g. The average yield when ligroin was used as a solvent was 64%.

The pyrazoline derivative is moderately soluble in boiling alcohol, sparingly in cold alcohol and ether, insoluble in ligroin. Its solutions in alcohols turn to a brilliant red color when a little hydrogen chloride is passed into them. On protracted heating below the temperature at which it decomposes it passes into an isomer that crystallizes in needles which are readily soluble in alcohol and ether and which melt at 102.5–103°. This substance is also formed in small quantities during the condensation of the unsaturated ketone and diazo ester, and accumulates in the mother liquors. It is probably a stereoisomer because its alcoholic solutions with hydrochloric acid give the same color as the higher melting product.

Calc. for $C_{19}H_{18}O_4N_2$: C, 70.8; H, 5.6. Found: C, 70.5; H, 5.6.

4,6-Diphenyl-pyrone-1,2,

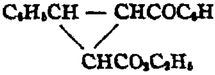


$$\begin{array}{l} C_6H_5C - CH = C - C_6H_5 \\ \quad\ \ \| \qquad\qquad\ | \\ \quad\ \ CH - CO - O \end{array}$$

.—This is always the principal product that is formed when the pyrazoline compounds are decomposed at high temperatures. It is most easily purified by first distilling the oily melt under diminished pressure and then recrystallizing the solid distillate from alcohol. It is very sparingly soluble in cold alcohol, readily soluble in ether and boiling alcohol, and crystallizes in yellow plates which melt at 138–139°.

Calc. for $C_{17}H_{12}O_2$: C, 82.3; H, 4.8. Found: C, 82.2; H, 5.0.

Ethyl 2-Phenyl-3-benzoyl-cyclopropane Carboxylate,



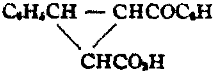
$C_6H_5CH - CHCOC_6H_5$ over $CHCO_2C_2H_5$.—The cyclopropane derivative is probably formed whenever the pyrazoline is decomposed at high temperature but the yield is always small, for we never got over 2% when the pyrazoline was heated by itself. In an effort to improve the yield we decomposed the substance under a variety of different conditions: in solution in high boiling liquids, under increased and reduced pressures, and in contact with charcoal, a variety of porous materials that promote gas reaction, platinized asbestos, and all the common metals. Of these only platinum and gold proved useful

The method of preparation finally adopted was therefore as follows: The pyrazoline was heated in a metal bath in 10 g. lots with 3 g. of platinum scrap to each lot. At 220–225° nitrogen was given off very rapidly and the decomposition was usually complete in 2–3 minutes. The resulting oil was dissolved in alcohol and the cyclopropane derivative allowed to crystallize slowly. The crystals were always yellow owing to contamination with a trace of the pyrone and several recrystallizations were necessary to get a colorless product. The average yield was 37%.

Calc. for $C_{19}H_{18}O_3$ C, 77.6; H, 6.1. Found C, 77.6; H, 6.1.

The cyclopropane ester crystallizes in thin plates and melts at 103°. It is readily soluble in boiling alcohol and in acetone. moderately soluble in cold alcohol, ether, benzene, and acetic acid. It does not reduce a solution of permanganate in acetone. In a good vacuum it can be distilled without loss and it was recovered unchanged after it had been heated above 300° for several hours.

2-Phenyl-3-benzoyl-cyclopropane Carboxylic Acid,



$C_6H_5CH - CHCOC_6H_5$ over $CHCO_2H$.—For the purpose of hydrolysis an excess of 2:3 aqueous potassium hydroxide solution was added to an alcoholic solution of the ester. After 10 minutes the solution could be diluted with water without becoming turbid—indicating complete hydrolysis. The solution was acidified, the curdy precipitate thoroughly washed with water, dried and dissolved in benzene. The solution first deposited a small quantity of fine needles, then the main product in long, thin filaments, like thistledown. These are two stereoisomeric acids.

The acid which crystallizes in needles is easily purified. It melts at 176°, and is very readily soluble in alcohol and ether, moderately in benzene, almost insoluble in ligroin.

Calc. for $C_{16}H_{14}O_3$: C, 76.7; H, 5.3. Found: C, 76.4; H, 5.4.

It is difficult to get the other acid in a form in which it will give a sharp melting point because it is always contaminated with a small quantity of its isomer. After a number of recrystallizations from benzene it melted at 147–150°.

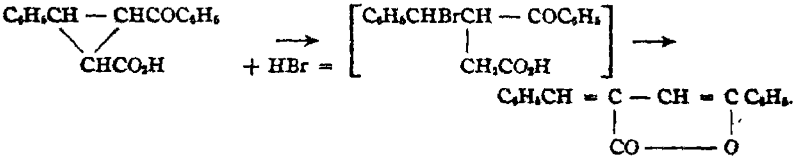
Calc. for $C_{16}H_{14}O_3$: C, 76.7; H, 5.3. Found: C, 76.5; H, 5.2.

Each of the cyclopropane acids was re-esterified by way of the silver salt and ethyl iodide. The higher melting acid gave the ester from which the acids had been obtained by hydrolysis. The lower melting acid gave an isomeric ester which melted at 93–94°. This crystallized from alcohol in stout needles and from ether in 6-sided plates.

Calc. for $C_{19}H_{18}O_3$ C, 77.6; H, 6.0. Found: C, 77.4; H, 6.0.

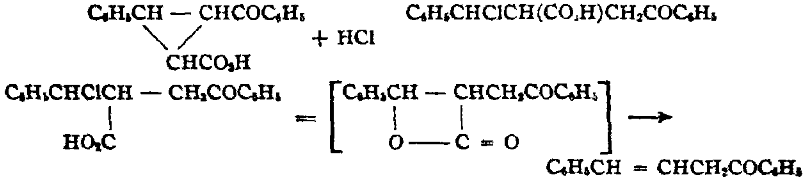
Action of Hydrobromic Acid on the Cyclopropane Acid.—In order to compare the behavior of this acid with that of the corresponding dibasic acid studied by Buchner, it was sealed up in a tube with excess of conc. aqueous hydrobromic acid. No reaction took place in the cold. The tube was therefore heated in a steam-jacketed furnace. It was extensively decomposed and gave only tarry products, while Buchner's acid under the same conditions remained unchanged.

For the purpose of comparing the behavior of the acid with those described in earlier papers, its solution in glacial acetic acid was saturated with hydrogen bromide. The solution turned yellow at once and in a few hours deposited a yellow crystalline solid, melting at 149–150°. This was identified as α-benzal-γ-phenyl-crotonic lactone by comparison with a specimen on hand. The acid, therefore in this respect, behaves exactly like the ketonic cyclopropane acids which contain two carboxyl groups, the ring opening between carbon atoms (2) and (3).



Action of Hydrogen Chloride.—A solution of the lower melting acid in glacial acetic acid was saturated with hydrogen chloride. It remained colorless and after a time deposited a colorless acid which melted with decomposition at about 131–132°, and contained chlorine. This acid was extremely unstable, losing both hydrochloric acid and carbon dioxide with the greatest ease. When dissolved in alcohol, however, it formed the corresponding ester which was perfectly stable. An analysis of the ester showed that the acid must have the composition $C_{17}H_{14}O_3Cl$, and, therefore, that it is formed by addition of a molecule of hydrogen chloride to the cyclopropane acid.

When this chloro acid was heated above its melting point for a few minutes it lost carbon dioxide and hydrochloric acid and gave a neutral, halogen-free product which melted at 92–93°. This was identical with the β-benzal-propiophenone which Wieland obtained by hydrolysis of α,δ-diphenyl-α-nitro-butadiene. Wieland's compound melted at 93° and gave an oxime that at 104° melted to a turbid liquid which became clear at 106°. Our product melted at 92–93° and gave an oxime which behaved exactly like Wieland's. Hydrochloric acid therefore adds in the manner assumed for hydrobromic acid, the proof being based on the following equations:



Ethyl α-Phenacyl-β,β-chloro-phenyl Propionate, $C_6H_5CHClCH(CO_2C_2H_5)CH_2COC_6H_5$.—The ester was obtained not only by dissolving the corresponding acid in alcohol but also and much more easily, by saturating an alcoholic solution of either the cyclopropane acid or its ester with hydrogen chloride. This is the first case that we have met in which a cyclopropane derivative combines with a halogen acid in alcoholic solution.

Calc. for $C_{19}H_{19}O_3Cl$: C, 69.0; H, 5.8. Found: C, 68.6; H, 6.1.

The ester crystallizes from alcohol in hexagonal plates which melt at 68–69°. Its most characteristic property is the ease with which it loses hydrogen chloride to potassium acetate and forms a cyclopropane derivative. Although it is a β-chloro ester, not a trace of ethylenic compound is formed in the process.

Reduction.—A solution of the cyclopropane ester in acetic acid was boiled with excess of zinc dust for half an hour. On cooling it deposited a flocculent ester which melted at 59–61°. For the purpose of identification this was hydrolyzed to the corresponding acid. It gave an acid melting at 152–154° which was identified as β-phenyl-γ-benzoyl-propionic acid by comparison with a specimen of this acid prepared in another way.[1]

Reaction with Acid Chlorides.—Both the cyclopropane acid and its ethyl ester were treated with thionyl chloride and with phosphorus pentachloride. The ester was not attacked by either reagent. The acid was transformed into the acid chloride but aside from a trace of yellow color there was no evidence that the ring was affected. Thus a solution of the acid in carbon tetrachloride was boiled with excess of phosphorus pentachloride until evolution of hydrogen chloride ceased. The pentachloride was then filtered off and the solvent evaporated under diminished pressure. It left a pale yellow oil. This, when dissolved in alcohol gave almost the calculated quantity of the ethyl ester. An attempt to use the acid chloride in a Friedel and Crafts reaction proved unsuccessful, the sole product being the same benzal-phenyl-crotonic lactone that had been previously obtained by the action of hydrogen bromide.

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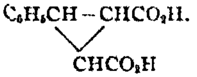
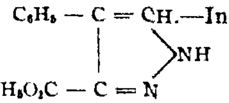
[1] *Ann.*, 46, 235 (1843).

Experiments with 3-Phenylcyclopropane Diacid-2,2,



—The acid and its ester were prepared by the method of Buchner. A solution of the ester in absolute alcohol was saturated with hydrogen chloride and allowed to stand at the ordinary temperature for several days. The ester was recovered unchanged. Solutions of the acid in glacial acetic acid were saturated with hydrochloric and hydrobromic acid and likewise allowed to stand for several days, but here also the original substance was recovered. It is evident, therefore, that the diacid is not affected by hydrochloric or hydrobromic acids, under conditions under which the acids produce ring cleavage in the corresponding ketonic acid.

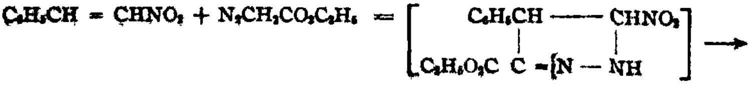
Ethyl 4-Phenyl-pyrazol-carboxylate-3,

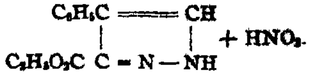


—In order to determine whether nitro-cyclopropane derivatives could be obtained from the corresponding pyrazolines, a mixture of diazo-acetic ester and β-nitro-styrene in molecular proportions was gently warmed on a steam-bath. The reaction which started soon became so vigorous that it had to be moderated by cooling. The resulting brown oil crystallized spontaneously in thin plates. Recrystallization from alcohol gave colorless plates melting at 164–165°.

Calc. for $C_{12}H_{12}O_2N_2$: C, 66.7; H, 5.6 Found: C, 66.7; H, 5.9.

Its composition indicated a pyrazol derivative. The ester was therefore hydrolyzed and the resulting acid, which melted at 252–253°, heated above its melting point until effervescence ceased. The product, after crystallization from alcohol, appeared in leaflets melting at 228°—the properties of 4-phenyl-pyrazol. The reaction between nitro-styrene and ethyl diazo-acetate is, therefore, represented by the equation





$$\begin{array}{lcl} C_6H_5C & = & CH \\ \quad | & & \;| \\ C_2H_5O_2C\;C & = N - & NH \end{array} + HNO_2.$$

The reaction was also tried in ligroin and in ether at the lowest temperature at which it would take place. In each oxides of nitrogen appeared soon after the reaction started and the only product was the pyrazol derivative.

Summary.

1. Four methods were tried for making cyclopropane derivatives having one ketonic and one carboxyl group in combination with the ring: decomposition of a ketonic cyclopropane diacid, eliminating hydrogen bromide from a γ-bromo-ketonic acid, removing bromine from an α,γ-dibromo ketonic acid, and decomposing a pyrazoline-ketonic ester. All these methods gave cyclic compounds, but only the last could be used for preparing a cyclopropane derivative.

2. Reagents that combine readily with α,β-unsaturated ketones also combine with this type of cyclopropane derivatives. The addition products are open chained saturated compounds.

3. Diazo-acetic ester readily combines with nitro-styrene; but the product loses nitrous acid so easily that a pyrazol derivative is obtained instead of the nitro-pyrazoline which is first formed.

CAMBRIDGE, MASS

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY.]

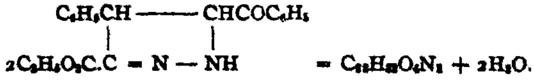
COLORED CONDENSATION PRODUCTS FROM KETONIC PYRAZOLINE DERIVATIVES.

BY E. P. KOHLER AND L. L. STEELE.

Received April 3, 1919.

The ketonic pyrazolines described in the previous paper give highly colored, fluorescent solutions in alcohol containing a trace of hydrochloric acid. We have isolated several of the products; they are high melting, sparingly soluble solids resembling the most brilliantly colored rhodamine dyes.

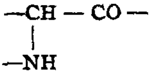
The pyrazoline derivative obtained by adding diazo-acetic ester to benzal-acetophenone gave a crimson product which was free from halogen. Its composition and molecular weight are represented by the formula $C_{40}H_{36}O_4N_4$. It is, therefore, formed in accordance with the equation



$$\begin{array}{lcl} & C_6H_5CH & - & CHCOC_6H_5 \\ & \quad | & & \;| \\ 2C_2H_5O_2C.C & = & N - & NH \end{array} = C_{40}H_{36}O_4N_4 + 2H_2O.$$

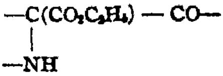
When the substance is allowed to remain in contact with a saturated solution of hydrochloric acid in alcohol, it takes up one molecule of the acid and one of water. The result is a yellow compound which readily loses both water and acid and reverts to the red product. In acetic acid the red compound combines with 2 molecules of water and forms a colorless compound which has the composition of the pyrazoline derivative but twice its molecular weight.

Similar products were obtained from all pyrazoline derivatives that had the grouping I, while a derivative which had the grouping II failed to give any color with hydrogen chloride.



$$\begin{array}{l}-CH-CO-\\ \;|\\ -NH\end{array}$$

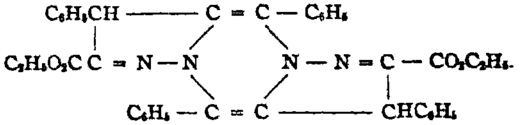
(I).



$$\begin{array}{l}-C(CO_2C_2H_5)-CO-\\ \;|\\ -NH\end{array}$$

(II).

The hydrogen α to carbonyl is, therefore, involved in the formation of the compound. This gives as a possible formula



Experimental Part.

When gaseous hydrogen chloride is passed into a concentrated solution of ethyl 4-phenyl-5-benzoyl-pyrazoline carboxylate-3 in alcohol, the solution turns red immediately but begins to fade again without depositing any solid material. If the solution is kept in ice-water while the gas is introduced, a crimson precipitate forms in small amount. When this is left in contact with the acid solution it redissolves and the color of the solution gradually fades. The red compound is evidently an intermediate product which has to be caught in passing.

The method of preparation finally adopted was as follows: hydrogen chloride was passed into 150 cc. of boiling methyl alcohol in which 20 g. of the ketonic pyrazoline was suspended as a fine powder. As soon as all of the pyrazoline had disappeared the precipitated crimson solid was filtered off and washed with alcohol. As no suitable solvent was found from which the substance could be recrystallized, it was purified by prolonged boiling with carbon disulfide. It was changed in the process from an impalpable powder to a mass of short, stout needles. After washing with ether these melted at 266–268°.

Calc. for $C_{38}H_{32}O_4N_4$: C, 75.0; H, 5.3. Found: C, 75.0; H, 5.2.

We failed to find any solvent in which the substance is sufficiently soluble for an accurate molecular-weight determination. Hot nitrobenzene dissolves about one g. of it per 100 g. of solvent and if this solution is allowed to cool without disturbance it generally retains the solute for several hours. The molecular weight found by freezing a somewhat more dilute solution than this was 525 instead of 608 calculated for the formula given.

The substance is so little soluble in alcohol and ether that it barely imparts a red tinge to the solutions. It is slightly soluble in benzene and carbon disulfide. The solutions are fluorescent; their color is a brilliant crimson-orange by reflected light, a rich purple by transmitted light. A specimen exposed to sunlight for 3 months, in a sealed tube, did not change either in color or melting point, but the dilute solutions in benzene acetone, and carbon disulfide soon faded to yellow in the light. The red compound is remarkably stable at high temperatures. In a vacuum it sublimes freely at about 400°.

Action of Hydrochloric Acid.—Hydrochloric acid was passed into a suspension of the red condensation product in alcohol. The red solid disappeared rapidly, the solution becoming at first greenish yellow and finally yellow. The alcohol, on evaporation, left a green powder which, after recrystallization from the same solvent, was obtained in yellow plates that melted to a red liquid at 258–259°.

Calc. for $C_{38}H_{33}O_5N_4Cl$: C, 68.8; H, 5.2; Cl, 5.4. Found: C, 68.9; H, 4.8; Cl, 5.9.

These results indicate that the yellow compound is formed by the addition of one molecule of water and one of hydrogen chloride to the condensation product. The substance gradually turns red both when heated by itself and when boiled with glacial acetic acid.

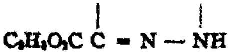
Action of Acetic Acid.—On protracted boiling with glacial acetic acid the red compound slowly dissolved and the solution finally became colorless. It was poured into water which precipitated a colorless product. By recrystallization from alcohol, this was obtained in small, colorless needles, which turned brown at about 170°, and melted to a clear brown liquid at 181°. The composition indicates that this compound is formed by the addition of 2 molecules of water to the red product.

Calc. for $C_{38}H_{34}O_6N_4$: C, 70.8; H, 5.6. Found: C, 70.8; H, 5.3.

Condensation Product from Ethyl 4-Phenyl-5(4-bromobenzoyl)-pyrazoline Carboxylate-3.—The condensation was carried out as with the bromine-free compound and the product purified in the same way. The brilliant purple-red needles melted at 268–270°.

Calc. for $C_{38}H_{28}O_4N_4Br$: C, 59.6; H, 3.9. Found: C, 60.1; H, 3.9.

Ethyl 4-Phenyl-5-benzalaceto-pyrazoline Carboxylate-3,



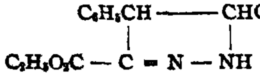
$$\begin{array}{l} C_6H_5CH \text{———} CH - CO - CH_2CHC_6H_5 \\ \quad\;\; | \qquad\qquad\quad | \\ C_2H_5O_2C\;C = N - NH \end{array}$$

—A mixture of 10 g. of dibenzal-acetone and 9.8 g. of ethyl diazo-acetate was heated in ligroin at 50–70° for several hours, then allowed to remain at the ordinary temperature for several days, during which the pyrazoline derivative separated in light yellow plates. It was purified by recrystallization from alcohol in which it is only sparingly soluble. Its melting point was 164.5–165°. The yield was small.

Calc. for $C_{21}H_{20}O_3N_2$: C, 72.4; H, 5.8. Found: C, 72.1; H, 5.9.

When hydrogen chloride was passed into an alcoholic solution of the pyrazoline derivative it soon produced a deep blood-red color, but no pure product could be isolated. The dilute solutions were red by transmitted and green by reflected light.

Ethyl 4-Phenyl-5-aceto-pyrazoline Carboxylate-3,



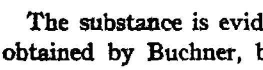
$$\begin{array}{lcl} & C_6H_5CH & \text{———} & CHCOCH_3 \\ & | & & | \\ C_2H_5O_2C - & C & = N - & NH \end{array}$$

—A mixture of 7 g. of benzal-acetone and 5.7 g. of ethyl diazo-acetate was heated at 75–80° for two hours, during which 2.5 g. of solid product separated. This was washed with ether in which it was almost insoluble and recrystallized from alcohol. It separated in white needles melting at 127°.

Calc. for $C_{14}H_{16}O_3N_2$: C, 64.6; H, 6.2. Found C, 64.8; H, 6.4.

A trace of hydrochloric acid in an alcoholic solution of the pyrazoline derivative produced an intense yellow color. More hydrochloric acid changed the color to orange and precipitated a small quantity of orange colored crystals. Dilute solutions of the condensation product were yellow by transmitted, and green by reflected light.

Ethyl 4-Phenyl-5-acetyl-pyrazoline Dicarboxylate-3,5,



$$\begin{array}{lcl} & C_6H_5CH & \text{———} & C(COCH_3)CO_2C_2H_5 \\ & | & & | \\ C_2H_5O_2C - & C & = N - & NH \end{array}$$

—The pyrazoline derivative was prepared according to directions given by Buchner[1] but for some reason we obtained a product melting at 105–106° instead of 76° as given by Buchner. Our product was sparingly soluble in alcohol and crystallized in fine needles.

Calc. for $C_{17}H_{20}O_5N_2$: C, 61.4; H, 6.1. Found: C, 61.2; H, 6.0.

The substance is evidently a stereoisomer of the pyrazoline derivative obtained by Buchner, because when it was heated to 270–290° it lost nitrogen and gave the same pyrone ester which Buchner had obtained by heating the product melting at 76°.

Hydrogen chloride was passed in the usual way into an alcoholic solution of the pyrazoline derivative but failed to produce any color, and only unchanged substance separated when the solution was allowed to cool.

CAMBRIDGE, MASS.

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[1] *Ber.*, 35, 785 (1902).

[CONTRIBUTION FROM THE HARRIMAN RESEARCH LABORATORY, THE ROOSEVELT HOSPITAL, IN COÖPERATION WITH THE SECTION OF FOOD AND NUTRITION, MEDICAL DEPARTMENT, U. S. ARMY.]

THE SUPPOSED OCCURRENCE OF METHYLGUANIDINE IN MEAT, WITH OBSERVATIONS ON THE OXIDATION OF CREATINE BY MERCURIC ACETATE.

BY ISIDOR GREENWALD.

Received March 18, 1919.

The experiments to be reported grew out of an attempt to investigate the nature of the toxic agent in "meat poisoning." Methylguanidine is one of the most toxic substances claimed to have been obtained from meat, or extract of beef, and it seemed possible that this compound might be a factor in such poisoning. The investigation is not complete, but sufficient evidence has been accumulated to indicate that methylguanidine is not present in meat, save, possibly, that which has undergone very extensive decomposition. The work is presented in its present form because it confirms the recently published work of others,[1] and because its resumption in the near future is not likely.

Methylguanidine was first obtained from physiological material by Brieger,[2] who used horse meat that had been allowed to decompose for 4 months, and by his pupil Hoffa,[3] and from the flesh of rabbits infected with "rabbit septicemia." They claimed that by their method they were unable to find any methylguanidine in fresh or normal meat. Their procedure was quite complicated and apparently was not used by other investigators. All other reports on the presence of methylguanidine in meat or in extract of beef are based on the use of either or both of the following methods of precipitation: (*a*) silver nitrate and barium hydroxide, (*b*) mercuric chloride and sodium acetate.

In 1916, Ewins[4] showed that creatine was oxidized to methylguanidine by means of silver oxide, and, that, consequently, all reports as to the presence of the latter which were based upon precipitation with silver nitrate and barium hydroxide were of little value. However, Ewins regarded precipitation with mercuric acetate as free from the danger of oxidation.

In the description of the method for the isolation of methylguanidine by means of precipitation with mercuric chloride and sodium acetate, there is mentioned a heavy white precipitate which is insoluble in hot, dil. hydrochloric acid. It seemed to the author that this could only be mercurous chloride, and that it was probably formed as a result of the oxidation of creatine.

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[1] Baumann and Ingvaldsen, *J. Biol. Chem.*, 35, 277 (1918).

[2] Brieger, *Untersuchungen über Ptomaine*, III, 1888, p. 33.

[3] Hoffa, *Sitzungsb. physikal. medizin. Ges. Würzburg*, 1889, p. 96; *Jahresb. Tierchem.*, 19, 472.

[4] Ewins, *Biochem. J.*, 10, 103 (1916).

Experiment proved that this was the case. Both methylguanidine and oxalic acid were isolated and identified as products of oxidation. The existence of an intermediate substance was suspected, but attempts at its isolation were not immediately successful. About 20% of the nitrogen of the creatine was obtained as ammonia (or other amine that could be completely distilled in a current of air at ordinary room temperature), indicating either that some methylguanidine was further oxidized, or that there was some other reaction in progress.

The work had reached this stage when the author was informed in a personal communication that Baumann and Ingvaldsen had also observed the oxidation of creatine by means of mercuric acetate and had isolated the substance intermediate between creatine and methylguanidine and oxalic acid. That work has since been published.[1] Baumann and Ingvaldsen called their new substance methylguanido-glyoxylic acid.

$$CH_3NHC(:NH)NHCOCOOH.$$

Its constitution was established by (1) derivation from creatine, (2) nitrogen content, and (3) hydrolysis in a solution of sodium acetate, precipitation with calcium chloride, filtration and ignition. The calculated quantity of calcium oxide was obtained.

The substance is unstable, decomposing readily upon evaporation of its solutions at ordinary pressures. Using diminished pressure, the substance was readily obtained and was found to have the properties described by Baumann and Ingvaldsen.

An attempt was made by the author to determine more completely its constitution. The substance which forms the insoluble calcium compound after hydrolysis was identified as oxalic acid by weighing the air-dried precipitate, then igniting and weighing again. The weights observed were those calculated from $CaC_2O_4.H_2O$ and for CaO.

TABLE I.

Analysis of α-Methylguanido-glyoxylic Acid.

Preparation No	Substance taken. G	CaC_2O_4 H_2O		CaO.	
		Found G.	Calculated G.	Found. G	Calculated. G.
I............	0 0906	0.0935	0.0915	0.0352	0.0350
	0.1916	0 1930	0.1988	0.0745	0.0741
II...........	0.1804	0.1840	0.1814	0.0710	0.0698
	0 1866	0.1885	0.1875	0.0734	0.0721
III..........	0.1770	0.1810	0.1782	0.0690	0.0684
	0 1608	0.1660	0 1619	0.0634	0.0621
IV...........	0 2231	0.2252	0.2246	0.0867	0.0862
	0 2392	0.2412	0.2409	Lost	..

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[1] Baumann and Ingvaldsen, *J. Biol. Chem.*, 35, 277 (1918).

It was also attempted to isolate methylguanidine from the products of hydrolysis of the substance. 0.33 g. was dissolved in water and evaporated to dryness after adding 3 cc. conc. hydrochloric acid. The residue was dissolved in water and treated with an excess of sodium picrate. There was obtained 0.243 g. of a substance having the characteristic crystal form of methylguanidine picrate and melting at 195° (uncorr.). The small yield is noteworthy. The theoretical yield is 0.665 g. It is probable that some other form of decomposition occurs. This may partly explain the failure to secure more than 50% of methylguanidine from creatine.

A typical protocol is presented. The methylguanido-glyoxylic acid was identified by melting point, nitrogen content and by hydrolysis and precipitation with calcium chloride, weighing as $CaC_2O_4.H_2O$ and as CaO. Methylguanidine was weighed as the picrate, which was identified by crystal form, melting point and yield of picric acid and of methylguanidine hydrochloride. For this purpose a weighed quantity of the picrate was dissolved in hot water, transferred to a continuous extraction apparatus, treated with hydrochloric acid and then extracted with benzene, using a weighed flask. After complete extraction, the benzene was distilled off, the flask dried at 105°, cooled and weighed. The acid solution was also evaporated, at first in a beaker, then in a small glass evaporating dish, dried at 105° and weighed. The calculated quantities of picric acid and methylguanidine hydrochloride were obtained.

13.1 g. creatine (4.2 g. nitrogen) was dissolved in 800 cc. water, and 225 g. mercuric acetate added. The mixture was allowed to stand at room temperature for 8 days and was then filtered. Ten cc. of this filtrate was used for a determination of creatine, and found to contain less than 0.1 mg. of this substance. The precipitate was then washed with cold water. The precipitate is known as Fraction I; the filtrate as Fraction II.

Fraction I.—The precipitate was suspended in water and decomposed with hydrogen sulfide. The mercuric sulfide was filtered out and the filtrate set aside. The precipitate was then washed with hot water and the washings allowed to cool, whereupon white crystals separated. These were kept, and the mother liquid and the filtrate previously obtained evaporated at about 15 mm. pressure to a small volume. The distillate was collected and tested for nitrogen. None was found. The liquid in the distilling flask yielded a second crop of crystals which was added to the first. After filtering, washing with cold water and drying at 115°, they weighed 5.133 g. They were identified as α-methylguanido-glyoxylic acid, as described previously. The filtrate was evaporated and yielded 1.058 g. of a substance containing 16.2% of nitrogen and melting at 135°. After recrystallizing from hot water, the melting point was

202°. The substance which melted at 135° was probably a mixture of methylguanido-glyoxylic acid (m. p. 203°) and oxalic acid.

The filtrate from these crystals contained 0.900 g. of nitrogen. Upon treatment with picric acid, methylguanidine picrate was obtained. The amount, however, accounted for only 0.495 g. of nitrogen.

Fraction II.—This was treated with hydrogen sulfide and mercuric sulfide filtered out and washed with hot water. No crystals were obtained on cooling or after evaporation *in vacuo*. The distillate was nitrogen free. The liquid in the distilling flask contained 1.68 g. nitrogen, of which 1.32 g. was accounted for as methylguanidine upon treatment with picric acid.

TABLE II.

Distribution of Nitrogen after Oxidation of 13.1 g. Creatine (4.20 g. Nitrogen) with Mercuric Acetate.

	Fraction I G.	Fraction II. G
Methylguanido-glyoxylic acid	1.490	...
Crystals melting at 135° (impure methylguanido-glyoxylic acid)	0.170	...
Methylguanidine	0.495	1.320
Nature unknown	0.405	0.360
Total	4.24 g.	

It is clear that precipitation with mercuric salts is not suited to the isolation of methylguanidine, not only because these oxidize creatine but also because they do not completely precipitate methylguanidine, as is evident from the preceding protocol. Nor is the matter helped by making the mixture alkaline. In one experiment, 0.934 g. of methylguanidine hydrochloride (equivalent to 2.58 g. of the picrate) was dissolved in water and treated with mercuric chloride and sodium hydroxide, keeping the mixture just alkaline to litmus. The precipitate was filtered out and dissolved in hydrochloric acid, the mercury removed with hydrogen sulfide, and the filtrate from the mercuric sulfide evaporated. Upon treatment with sodium picrate, only 1.101 g., or less than half of the calculated quantity of methylguanidine picrate, was obtained. It is evident that the method offers no possibilities, even if creatine could be quantitatively removed before treatment with mercuric salts.

Many other procedures were tried, but none was satisfactory. The best results were obtained with a technique which is based upon the same principles as is Brieger's, but differs in certain details.

The hashed meat was suspended in about twice its weight of water, and was heated to boiling and filtered through muslin. The filtrate was set aside and the residue was again extracted. This process was repeated. The extracts were separately precipitated with basic lead acetate solution. The next day the precipitate in the first extract was removed by centrifugation, and was suspended in the second extract. This was repeated the next day for the third extract, serving to economize in wash water and in the time required to evaporate it. The liquid was then evaporated at about 10 mm. pressure to a volume of about 100 cc. per kg. of meat, and was then poured into about two volumes of alcohol. The next day the precipitate was filtered out, washed with alcohol, and the filtrate was treated with hydrogen sulfide. The lead sulfide was removed, washed with alcohol, and the filtrate treated with 2 or 3 cc. of a saturated alcoholic solution of zinc chloride to remove creatinine. After 2 or 3 days in the ice-chest, the precipitate was filtered out, and the filtrate was treated with an alcoholic solution of mercuric chloride until precipitation was complete. After standing overnight, this precipitate was filtered out, and the filtrate treated with hydrogen sulfide. The filtrate from the mercuric sulfide was evaporated to small volume and precipitated with alcohol. The insoluble portion was rejected, the filtrate and washings were again evaporated and precipitated with absolute alcohol. This was repeated until the residue was practically entirely soluble in absolute alcohol. Water was then added, the alcohol boiled away, and the bases remaining precipitated with hydrochloric and phosphotungstic acids. The next day this precipitate was washed with a dilute solution of hydrochloric and phosphotungstic acids, and then decomposed with barium hydroxide in the cold. The filtrate from the barium phosphotungstate was acidified with hydrochloric acid and evaporated to small volume. Four or five volumes of 95% alcohol were then added and the mixture allowed to stand overnight. The precipitate was filtered out, washed with alcohol, the filtrate evaporated and the treatment with alcohol repeated until all was soluble in absolute alcohol. Water was added, the alcohol boiled away, and sodium picrate added. After standing on ice overnight, the precipitate was filtered out, dissolved in hot water, filtered and allowed to crystallize.

If any considerable amount of the precipitate was obtained it was filtered out, dried and weighed. Some was taken for a melting-point determination. The remainder was dissolved in hot water, decomposed with hydrochloric acid and extracted with benzene, in a continuous extraction apparatus. The benzene was evaporated and the picric acid weighed. The acid liquid was also evaporated in a weighed dish and the residue of methylguanidine hydrochloride(?) weighed.

In all, 3 lots of beef that had been standing at room temperature for 3 or 4 days were used. With two of these, very good results were obtained. In each case, two samples were taken. To one was added a weighed quantity of methylguanidine hydrochloride (obtained from a weighed quantity of the picrate); the other was used as a control. In both cases the latter yielded a negligible amount of picrate, while the added methylguanidine was recovered, quantitatively, as the picrate and identified as already described. Protocols follow:

Expt. V. June 24, 1400 g. of beef used. 0.005 g. picrate obtained.

Expt. VI. June 25, 1400 g. of the same beef used. Added 0.808 g. methylguanidine hydrochloride (equivalent to 2.23 g. of the picrate). Obtained 1.65 g. of picrate which melted at about 195° and which yielded 1.24 g. of picric acid and 0.621 g. of hydrochloride. (Calculated for methylguanidine picrate 1.25 and 0.600 g., respectively.)

Expt. VII. July 12, 1400 g. of another sample of meat used. 0.015 g. of dark picrate obtained.

Expt. X. July 19, 1400 g. of the same sample of meat as used in Expt. VII. Added 0.475 g. methylguanidine hydrochloride (equivalent to 1.33 g. of the picrate). Obtained 1.35 g. of picrate which melted at about 195° and which yielded 1.06 g. of picric acid and 0.517 g. of hydrochloride. (Calculated for methylguanidine picrate 1.02 and 0.490 g. respectively.)

The latter experiments were much less satisfactory. A considerable amount of insoluble picrate was obtained, but analysis showed that this was not methylguanidine picrate but some other substance. The protocols follow:

Expt. XI. July 24, 1400 g. meat used. Obtained 0.6445 g. picrate decomposing at about 190°. This yielded 0.4244 g. picric acid and 0.2755 g. of hydrochloride. (Calculated for methylguanidine picrate 0.488 g. and 0.233 g., respectively.) The hydrochloride was dissolved in water, and aliquots taken for nitrogen determinations. The total was 0.0642 g. If the original substance had been methylguanidine picrate 0.0895 g. was to be expected. The remainder of the solution was treated with sodium picrate. A picrate melting at 205° was obtained. Since this is considerably higher than the melting point (198°) of the purest methylguanidine picrate which had been obtained, it is obvious that the two are not identical.

Expt. XII. July 25, 1400 g. of the same meat used, with the addition of one g. creatine. Obtained 0.6545 g. picrate, decomposing at about 190°. Analysis lost.

Expt. XIII. July 27, 750 g. of the same meat used. Added 0.095 g. methylguanidine hydrochloride (equivalent to 0.266 g. of the picrate). Obtained 0.9066 g. of the picrate decomposing at 205° and yielding 0.6553 g. picric acid and 0.3372 g. hydrochloride. (Calculated for methylguanidine picrate 0.687 and 0.337 g., respectively.) The hydrochloride was treated as in Expt. XI. Calculated 0.126 g. nitrogen. Found 0.078 g. The remainder of the solution was treated with sodium picrate. A picrate melting at 210° was obtained.

It is probable that the poor results of these last experiments were due to faulty technique. However, it is believed that sufficient evidence has been presented to demonstrate that methylguanidine is not present in meat that is in a fair state of preservation. Whether or not it is present in badly decomposed meat has not been determined. That may depend upon the nature of the organisms responsible for the decomposition. Falk, Baumann and McGuire[1] have found that the creatine of meat is resistant to the action of the bacilli of the paratyphoid group, which is the type commonly found in "meat poisoning."[2,3] In any event, methylguanidine can scarcely be regarded as playing an important part in the mechanism of "meat poisoning" for such poisoning is due to meat that is not badly decomposed. The nature of the toxic agent will be considered in another paper.

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[1] Falk, Baumann and McGuire, *J. Biol. Chem.*, 37, 525 (1919).

[2] Jordan, *Food Poisoning*, Univ. Chicago Press, 1917.

[3] Hübener, *Fleischvergiftungen und Paratyphusinfektionen*, G. Fischer, Jena, 1910.

NEW YORK, N. Y.

[CONTRIBUTION FROM THE ESSENTIAL OILS LABORATORY, DRUG DIVISION, BUREAU OF CHEMISTRY.]

THE CONSTITUTION OF CAPSAICIN, THE PUNGENT PRINCIPLE OF CAPSICUM.

BY E. K. NELSON.

Received April 11, 1919.

The pungent principle of Capsicum was first isolated by Thresh,[1] who assigned to it the name capsaicin. Thresh, however, did not throw any light on the constitution of the substance and overlooked the presence of nitrogen, giving the formula $C_9H_{14}O_2$.

Micko[2] improved the method of extracting capsaicin and obtained it as a crystalline substance of extreme pungency, melting at 63.5° and possessing the properties of a phenol. On the basis of analyses and molecular-weight determinations, he ascribed to it the formula $C_{18}H_{28}NO_3$. This is an impossible formula. His analyses agree well with the formula $C_{18}H_{27}NO_3$. Micko found one hydroxyl and one methoxyl group. He prepared a benzoyl derivative, melting at 74°, which was not pungent. On treating an alcoholic solution of capsaicin with platinic chloride and hydrochloric acid and allowing the mixture to evaporate spontaneously he noted a vanilla-like odor This suggests the presence of a vanillin residue in capsaicin.

Micko isolated capsaicin from paprika (*Capsicum annuum*) and from cayenne pepper (*Capsicum fastigiatum*). From one kg. of cayenne pepper he extracted 5.5 g. of crude capsaicin, which was 20 times the amount he found in paprika.

Nelson[3] extracted capsaicin by Micko's method and obtained 2.13 g. of the pure crystalline substance, melting at 64.5°, from 1.5 kg. of African capsicum.

Preparation of Capsaicin.

In order to prepare material for this investigation Micko's method of extraction was used. A considerable difference was observed in the amounts of capsaicin recoverable from different lots of cayenne pepper obtained on the market. In one case, only 12 g. of crude capsaicin was obtained from 40 pounds of the pepper. From 50 pounds of a very hot cayenne pepper 77 g. of crude capsaicin was obtained, which, on recrystallizing 3 times, yielded about 50 g. of the pure substance, melting at 65°. Capsaicin is purified by crystallizing from petroleum ether containing 10% of ethyl ether. An alcoholic solution of capsaicin was found to be optically inactive.

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[1] *Pharm. J. and Trans.*, [3] 7, 21, 259, 473 (1876–77); 8, 187 (1877–78).

[2] *Z. Nahr. Genussm.*, 1, 818 (1898); 2, 411 (1899).

[3] *J. Ind. Eng. Chem.*, 2, 419 (1910).

Optical Crystallographic Data.[1]—*In ordinary light,* under the microscope, capsaicin shows overlapping plates which have, in part, rectangular outlines, but which break up readily into angular irregular fragments. The crystal system is probably monoclinic. Refractive indices $[{}^{20}_{\mathrm{D}}]$ (determined by the immersion method in potassium-mercuric iodide solutions): $\alpha = 1.520$, $\beta = 1.540$, $\gamma = 1.580$, $\gamma - \alpha = 0.060$, all $\pm$ 0.005. α and β are most often obtained, but γ is not difficult to find. *In parallel polarized light:* The birefringence is strong, moderately thin plates showing lower second order colors, although thin ones show first order grays. Extinction on rectangular plates is parallel to the edges, but on those tilted up seems to be inclined, reaching 20°. There is not definite elongation. *In convergent polarized light:* Partial biaxial figures are frequently visible, the axial angle being moderate in size, $2E$ = about 50° The sign is positive and the dispersion rather strong, with $2E_r < 2E_v$.

EXPERIMENTAL.

Methyl Capsaicin.

In order to stabilize capsaicin so that it would yield definite products on oxidation, the hydroxyl was methylated. Capsaicin (1.42 g.) was dissolved in 25 cc. of 5% sodium hydroxide solution, 3 cc. of dimethyl sulfate added, and the mixture shaken for 30 minutes. 10 cc. of 5% sodium hydroxide solution was then added to dissolve unchanged capsaicin and the methyl compound was separated by filtration and recrystallized from dil. alcohol. The yield was 1.46 g., or 98.3%. Methyl capsaicin is only moderately pungent, melting at 77–78°. Determination of methoxyl groups by Zeisel's method:

Subs., 0.2043, 0.2507: AgI, 0.2978, 0.3625.
Calc. for $C_{17}H_{23}NO(CH_3O)_2$: CH_3O, 19.31. Found: 19.26, 19.10.

Optical Crystallographic Data.—*In ordinary light,* methyl capsaicin is found to consist of minute needles more or less grouped into bundles, and curved or bent. The crystal system appears to be monoclinic. Refractive indices $[{}^{20}_{\mathrm{D}}]$ (determined by the immersion method in potassium-mercuric iodide solutions): $\alpha = 1.55$, $\beta = 1.58$, $\gamma = 1.60$, $\gamma - \alpha =$ 0.05, all $\pm$ 0.01. β is usually obtained lengthwise, and a mean of α and γ crosswise. *In parallel polarized light:* The birefringence is strong, high first order colors, white to yellow, being shown even by rather slender needles. The extinction is strongly inclined, reaching practically 45°. The elongation is mostly negative. *In convergent polarized light:* The crystals are too minute to yield definite figures, but the class is clearly biaxial.

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[1] The crystallographic measurements in this paper were made by Dr. Edgar T. Wherry, of the Bureau of Chemistry.

Oxidation of Methyl Capsaicin.

Methyl capsaicin (1.46 g.) was suspended in 50 cc. of 2 *N* sodium carbonate solution and to the mixture, boiling under a reflux condenser, 190 cc. of 3% potassium permanganate solution was slowly added. Ammonia was evolved. The solution was filtered from manganese dioxide, concentrated and acidified, when a difficultly soluble acid separated, which was recrystallized from boiling water. The yield was 0.4 g. The melting point of the dry acid was 180–181°. Admixture with veratric acid caused no depression in the melting point. On titration with alkali 0.333 g. required 3.66 cc. of 0.5 *N* sodium hydroxide giving 182 as the neutralizing equivalent.

Calc. for $C_9H_{10}O_4$: C, 59.31; H, 5.48. Found: C, 59.23; H, 5.55.

Veratric acid is therefore a product of the oxidation of methyl capsaicin, which indicates that a vanillin residue is present in capsaicin.

In addition to veratric acid, volatile acids appear to be formed, but, as the amount was small, they were not investigated at this time.

Acid Hydrolysis of Methyl Capsaicin.

As capsaicin and methyl capsaicin appear to resist the action of acids and alkalies remarkably well at ordinary temperatures, the hydrolysis of methyl capsaicin was conducted in an autoclave.

Methyl capsaicin (2.5 g.) was dissolved in 125 cc. of 50% methyl alcohol and 5 cc. conc. hydrochloric acid added. The solution was heated at 125° for 3 hrs. Alcohol and volatile substances were then removed by steam distillation and the acid solution, after extraction with ether to remove a small amount of unchanged methyl capsaicin, was evaporated to dryness, leaving a crystalline residue amounting to 1.35 g. This was recrystallized from hot alcohol. Analysis:

Subs., 0.2016: AgCl, 0.1419.
Subs., 0.1427: CO_2, 0.2776; H_2O, 0.0914.
Calc. for $C_9H_{13}NO_2HCl$: C, 53.04; H, 6.92; N, 6.87; Cl, 17.43. Found: C, 53.05; H, 7.14; N, 6.82; Cl, 17.39.

This substance proved to be identical with the hydrochloride of veratryl amine (3,4-dimethoxy-benzylamine hydrochloride), described by Juliusberg,[1] as no depression in melting point was observed on admixture with the hydrochloride of veratryl amine prepared by reducing methyl-vanilline oxime. A crystallographic examination also shows the compound to be the same.

Optical Crystallographic Data.—*In ordinary light*, 3,4-dimethoxybenzylamine hydrochloride is seen to be well crystallized in rods and narrow plates. The crystal system is monoclinic. Refractive indices $[^{20}_{D}]$ (determined by the immersion method in organic liquids): $\alpha = 1.505$, $\beta = 1.670$, $\gamma = 1.700$; $\gamma - \alpha = 0.195$, all ± 0.005. Those usually obtained are β and intermediate values between α and γ. *In parallel polarized light:* The birefringence is extreme, the colors being mostly of the fourth order. The extinction of the plates may be straight, but when they are tilted up to any extent is strongly inclined, reaching 40°. The elongation is either positive or negative. *In convergent polarized light:* Partial biaxial figures are seen on practically all of the plates, one optic axis being nearly perpendicular to them. The plane of the optic axes lies perpendicular to the surface of the plates, and parallel to their long sides. The acute bisectrix is, however, very difficult to obtain, as it lies at an angle of about 40° from the perpendicular to the plates. The axial angle 2E is about 60° and the sign negative. Dispersion is rather weak, with $2E_r < 2E_v$.

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[1] *Ber.*, 40, 120 (1907).

From the distillate containing volatile products of hydrolysis, ether extracted a pleasant-smelling oil which proved to be an ester formed by the action of methyl alcohol on an acid product of hydrolysis. The yield of this ester was small, on account either of loss from the autoclave, which was not quite tight, or of chemical changes. It was later found that the acid could be better isolated by an alkaline hydrolysis.

Acid Hydrolysis of Capsaicin.

The conditions under which the acid hydrolysis of capsaicin was carried out were identical with those described for methyl capsaicin. A crystalline hydrochloride was obtained, from which the free base was separated by dissolving in water and adding just sufficient 10% sodium hydroxide solution to neutralize the hydrochloric acid. The liberated base separates rapidly in needles, which, freed from water of crystallization, melt at 132–133°. On admixture with 3-hydroxy-4-methoxybenzylamine (vanillyl amine), the synthesis of which will be described later, no depression in melting point occurs. The crystallographic properties of the hydrochloride are identical with those of vanillyl-amine hydrochloride.

Synthesis of Vanillyl-amine.

Vanillin oxime (7 parts by weight) is dissolved in 20 parts of alcohol and reduced with 160 parts of 2.5% sodium amalgam, 14 parts of glacial acetic acid being gradually added, so as to maintain an acid reaction in the mixture. The temperature of the reaction should not exceed 50–60°. The mixture is diluted with water and extracted with ether to recover unchanged oxime. An excess of hydrochloric acid (sufficient to liberate all the acetic acid and convert the base into a hydrochloride) is then added, and the solution is evaporated to dryness. The hydrochloride of the base is dissolved in boiling absolute alcohol and filtered from sodium chloride. It crystallizes from the alcohol on cooling and is recrystallized from boiling alcohol. The yields averaged about 65%.

Optical Crystallographic Data.—*In ordinary light,* 3-hydroxy-4-methoxybenzylamine hydrochloride (vanillyl-amine hydrochloride) crystallizes in rods which break up into angular fragments. System probably monoclinic. Refractive indices $[^{20}_{\mathrm{D}}]$ (determined by the immersion method in organic liquids): $\alpha = 1.510$, $\beta = 1.705$, $\gamma = 1.735$, $\gamma - \alpha = 0.225$, all ± 0.005. α is frequently seen in one direction, and an intermediate value between β and γ in the other. *In parallel polarized light:* The birefringence is extreme, most of the grains showing pale hues of the fourth or fifth order. Extinction is often inclined, reaching a maximum of 35°. Elongation is usually negative. *In convergent polarized light:* Partial biaxial figures are often seen. The axial angle is moderately large, $2E = 70°$. The sign is negative. Dispersion is strong, with $2E_r < 2E_v$.

The free base is isolated by adding to a solution of the hydrochloride in lukewarm water an amount of 10% sodium hydroxide solution just sufficient to neutralize the hydrochloric acid. An excess will unite with the phenolic hydroxyl and redissolve the base. On standing, the base separates almost completely in fine needles, and, being very slightly soluble in water, can be washed on the filter. The melting point of the dried crystals is 131–133°. The material for analysis was dried at 110°.

Subs., 0.1903, 0.1592: CO_2, 0.4399, 0.3652; H_2O, 0.1220, 0.1056.

Calc. for $C_8H_{11}NO_2$: C, 62.70; H, 7.24; N, 9.14. Found: C, 62.98, 62.56; H, 7.12, 7.36; N, 9.11, 9.07.

The crystals of vanillyl amine, freed from adhering moisture by drying in a desiccator, weighed and dried to constant weight at 110°, lost weight equivalent to two molecules of water.

Free vanillyl amine is very unstable, being easily decomposed by caustic alkalies and even by boiling water. In a dry form it keeps very well in the dark. In the light it gradually becomes yellow.

Optical Crystallographic Data. — 3-Hydroxy-4-methoxy-benzylamine (vanillyl amine) is unsuited to complete optical characterization, as it is decidedly unstable, losing its water of crystallization at once on removal from the saturated aqueous solution. The following properties could be observed, however, on the crystals suspended in such a solution: *In ordinary light:* Crystallized in rods, probably belonging to the rhombic system. Refractive indices could not be determined. *In parallel polarized light:* The birefringence is very strong, second order colors being exhibited. The extinction is straight, and the elongation positive. *In convergent polarized light:* Biaxial, but definite figures are rarely obtained, the acute bisectrix being apparently the long axis of the rods.

Alkaline Hydrolysis of Capsaicin.

Twenty g. of capsaicin was mixed with 80 cc. of 25% sodium hydroxide solution and heated in a nickel vessel to 180° in an autoclave for 30 minutes. Ammonia was split off and the base was decomposed but the acid (previously detected as a product of acid hydrolysis) was almost quantitatively recovered. The reaction mixture was diluted with water, saturated with carbon dioxide, and extracted with ether. A quantity of resinous and colored products of the decomposition of vanillyl amine is thus separated.

The alkaline solution has a dark color, due, no doubt, to the presence of pyrocatechin or other phenolic decomposition products from the amine. It was evaporated to dryness and the sodium salt of the acid separated from sodium carbonate by boiling alcohol.

The residue left on evaporating the alcohol was dissolved in water, acidified with dil. sulfuric acid and distilled with steam. This operation required some time, as the acid distils slowly with steam. The distillates were extracted with ether and the solvent carefully evaporated. The yield was 11.1 g.

The acid was purified by distillation from a small flask at atmospheric pressure. It distils without decomposition at 258–261° (corr.). On titration with alkali, 0.5339 g. required 6.21 cc. 0.5 *N* sodium hydroxide, giving 172 as the neutralizing equivalent.

Subs., 0.1583, 0.1248, 0.1296: CO_2, 0.4075, 0.3231, 0.3338; H_2O, 0.1517, 0.1213, (lost).

Calc. for $C_{10}H_{18}O_2$: C, 70.53; H, 10.66. Found: C, 70.20, 70.60, 70.24; H, 10.74, 10.88.

The acid absorbs two atoms of bromine, yielding a dibromide, which, recrystallized from ethyl acetate, melts at 57–59°.

Hydrogenation by Paal's method, using colloidal palladium, showed 2.018 g. of the acid to absorb about 250 cc. of hydrogen (reduced to 0° and 760 mm.). The absorption was very slow and continued for 30 hours. The theoretical absorption for one double bond in $C_{10}H_{18}O_2$, using 2.018 g. of substance, is 264.8 cc. at 0° and 760 mm. The acid therefore absorbs two atoms of hydrogen, and is a decylenic acid.

The boiling point of the saturated acid obtained by hydrogenation is about 260°, and its melting point 24–25°. Admixture with capric acid from coconut oil causes immediate liquefaction. Therefore the saturated acid formed on hydrogenating the acid from capsaicin is not capric acid but an isomeric decylic acid.

The amide of the acid obtained from capsaicin is a beautifully crystalline substance. It was prepared in the following manner: 1.2 g. of the acid was mixed with 0.4 g. of phosphorus trichloride and allowed to stand for 12 hours. It was then added drop by drop to 7.5 cc. of conc. ammonium hydroxide, cooled in a mixture of ice and salt. The amide, which separated, was washed with 2% sodium hydroxide solution and recrystallized from dil. alcohol. The melting point was 96–97° (corr.)

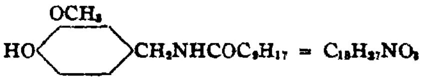
Optical Crystallographic Data.—The amide of the decylenic acid from capsaicin forms beautifully pearly leaflets which are not, however. adapted for optical crystallographic measurement. *In ordinary light,* it is seen to be crystallized in overlapping plates, without definite crystal outline. The mean refractive index (determined by the immersion method in organic liquids) is approximately 1.55. *In parallel polarized light:* The birefringence is weak, only blue-gray interference colors being shown. There is no definite elongation nor extinction. *In convergent polarized light,* the crystals yield a somewhat hazy, biaxial interference figure, with the axial angle 2E about 60° and the sign positive.

The decylenic acid from capsaicin crystallizes when cooled in a mixture of ice and salt and melts at about —5°. It is scarcely soluble in water and the silver and barium salts are insoluble in cold, and very difficultly soluble in boiling water.

A decylenic acid was prepared by Wallach[1] from menthone oxime, and found to boil at 257–261°, but the melting point of the amide (104–105°) differs from that of the decylenic acid from capsaicin. Wallach[2] has also prepared a decylenic acid from tetrahydro-carvone isoxime. This acid boils at 257–260°, but the amide melts at 63–64°. The recorded data on other decylenic acids are so meager that the identity of the acid from capsaicin with some one of them can, at the present time, be neither established nor disproved.

Constitution of Capsaicin.

Capsaicin is a condensation product of vanillyl amine (3-hydroxy-4-methoxybenzylamine) and a decylenic acid. Its constitution is therefore represented by the following formula:



The synthesis of substances analogous to capsaicin is at present in progress. Some of the substances thus far prepared are extremely pungent. Their description is reserved for a later communication.

The writer is indebted to Dr. Joseph A. Ambler, of the Bureau of Chemistry, for helpful suggestions.

WASHINGTON, D. C.

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[1] *Ann.*, 278, 312 (1894); 296, 120 (1897); 312, 199 (1900).

[2] *Ibid.*, 312, 204 (1900); 323, 325 (1902).

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF ELI LILLY & COMPANY.]

THE PREPARATION OF 1,2-DICHLORO-ETHER.

BY E. A. WILDMAN AND HAROLD GRAY.

Received April 28, 1919.

An investigation which was recently carried on involved the use of 1,2-dichloro-ether, a substance which is not available on the market. An examination of the literature showed that the best method of preparation was probably, by direct chlorination of ether, a method used by Fritsche and Schumacker,[1] although they did not give sufficient details to enable one to carry out the operation successfully.

The ease with which chlorine and ether react is shown by the fact that a mixture of the two in gaseous form may ignite spontaneously. If a flask is filled with chlorine at room temperature and one or two cc. of ether poured in, there will usually follow within a moment a slight explosion with ignition of the ether and the deposition of a quantity of soot. If during the chlorination of ether, particularly at the first, the temperature is not kept low by cooling with an ice-water bath, and the chlorine run in slowly, there is likely to be an accumulation of chlorine above the liquid which will result in the sudden ignition of the whole mass. As the reaction progresses, the ether becomes saturated with hydrogen chloride which decreases its inflammability and cooling is no longer necessary. The rate of passing in chlorine may also be much increased for the reaction takes place more rapidly than at first.

There is another difficulty which enters when the ether becomes saturated with hydrogen chloride. The latter seems to dissolve to the extent that it forms a supersaturated solution when it suddenly escapes with almost explosive violence, carrying the ether along with it. In one case when 6 liters of ether were being chlorinated in a large wide-mouthed bottle the entire contents with the exception of about 500 cc. was ejected as if from a geyser. Occasional agitation of the material was not sufficient to prevent this. It was found necessary to agitate continuously by means of a rapidly revolving mechanical stirring device.

The operation was carried out as follows:

A two-liter flask was provided with a return condenser, an inlet tube for chlorine and an efficient stirring device connected by means of an oil seal in order that the escaping hydrogen chloride would be forced to go through the condenser. 800 g. of dry ether was placed in the flask and kept cold by a surrounding bath of ice and water. The ether was stirred from the beginning. After passing in a slow stream of chlorine for 35 hours the specific gravity was 0.785 at 25° and hydrogen chloride began to be evolved freely. The temperature was then allowed to rise gradually to that of the room. At the end of 65 hours the specific gravity was 0.89, and after 82 hours, 0.96. Chlorination was stopped at this point.

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[1] *Ann.*, 279, 301 (1894).

The unchanged ether was distilled off under reduced pressure and the remaining material fractionated. There was obtained 375 g. of dichloroether, boiling from 66 to 69° at 45 mm., representing a yield of 24.2% of the theoretical amount. The material in the distilling flask remained colorless till near the end, when it became black and there was left a small residue of 65 g.

It had previously been determined that chlorination should be stopped at about the point where the specific gravity was 0.96. In one trial during which it was carried on to the specific gravity 1.11 it was impossible to separate a pure fraction of dichloro-ether from the product.

INDIANAPOLIS, INDIANA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY, No. 322.]

ACTION OF ENZYMES UPON STARCHES OF DIFFERENT ORIGIN.

BY H. C. SHERMAN, FLORENCE WALKER AND MARY L. CALDWELL.

Received May 5, 1919

O'Sullivan,[1] working with malt extract and precipitated malt diastase, reported that potato starch was less readily digested to maltose than were the starches of the cereal grains when all were gelatinized by heating in water at 97° and tested under like conditions.

Stone,[2] also working with malt extract, judging the action by the disappearance of the blue coloration with iodine, found potato starch more digestible than wheat starch, and maize starch less so than either. With saliva, Stone found potato starch more digestible than the cereal starches, and among the latter maize and rice starches appeared more digestible than that of wheat. Stone also reported potato starch more readily digestible than cereal starches by pancreatin and by taka-diastase.

Ford[3] found the purified starches of rice, barley, maize, wheat, potato and arrow root when similarly prepared to be equally digested by malt extracts and attributed the differences found by other observers to the probable impurities in their starches.

In view of the conflicting results thus shown by the earlier work and the fact that previous observers have in general worked with but few forms of amylase and these usually with no attempt at isolation, a more comprehensive study which should include observations upon purified enzyme preparations, as well as secretions and extracts, seemed desirable.

[1] O'Sullivan, *J. Chem. Soc.*, **85**, 616 (1904).

[2] Stone, U. S. Dept. Agr., Office of Expt. Sta., *Bull.* 34.

[3] Ford, *J. Soc. Chem. Ind.*, **23**, 414 (1904)

The present investigation includes experiments upon the hydrolysis of wheat, maize, rice and potato starches by means of saliva, pancreatin, purified pancreatic amylase, malt extract, purified malt amylase, taka-diastase, and purified amylase of *Aspergillus orysae*.

Earlier investigations in this laboratory have shown that, at least with some amylases, the results of comparisons based upon disappearance of material giving blue coloration with iodine are apt to be misleading.[1] On the other hand, the gravimetric method which we have commonly employed for the determination of the amount of reducing sugar formed from "soluble" starch was not applicable because of the difficulty in filtering the starch dispersions here studied. We therefore adopted the method of allowing the enzyme to act upon a 1% dispersion of boiled starch for 30 minutes at 40°, employing in each series of measurements such an amount of the enzyme solution as would result in the formation of about $^1/_3$ to $^1/_2$ of the theoretically possible amount of maltose, and finally determining the reducing sugar formed by titration against Fehling's solution according to the well known volumetric method.

The general plan of our work has been to obtain or purify each starch by several methods and to compare the digestibility or rate of transformation into maltose of different starches when prepared by the same method and purified in the same manner and under the same conditions.

Starches.—The starches used in these experiments were prepared in the laboratory from wheat flour, corn meal, white rice, and mature potatoes. Each of the 4 starches was prepared in 4 different ways: (1) washing with water only, (2) with very dilute alkali, (3) with ether after washing with water, (4) with ether after washing with alkali.

In the preparation of starch from wheat flour or corn meal, the material was mixed with distilled water to a stiff dough and kneaded in a cheesecloth bag under distilled water. The starch suspension was then filtered through 4 thicknesses of cheesecloth to remove particles of cellulose or flocks of insoluble protein, then the starch allowed to settle and washed 5 times by decantation with distilled water. A portion of each of these starches was then stirred thoroughly with cold 0.3% solution of sodium hydroxide and allowed to stand overnight at ice box temperature after which the alkaline liquid was decanted and the starch washed 4 times by decantation with ordinary distilled water and twice with the triply distilled water especially prepared for our enzyme work. In the case of wheat starch a second portion was washed with a more dilute alkali, 0.15% instead of 0.3% sodium hydroxide solution; and a duplicate portion of the corn starch received two treatments with 0 3% sodium hydroxide solution, the subsequent washings with water being as stated above in all cases.

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[1] Sherman and Schlesinger, THIS JOURNAL, 35, 1784 (1913).

Rice starch was obtained by mixing finely ground, white rice with water and filtering through cheesecloth, then washing with water, 0.3% sodium hydroxide solution, water and triply distilled water as just described for the wheat and corn starches.

Potato starch was prepared from pared and grated potatoes by filtering and washing as in the preparation of the cereal starches.

After final washing, the starches were filtered on Büchner funnels by suction, dried first at room temperature and then in dry air at 30 to 40°. Portions of the water-washed and alkali-washed starches were then washed with ether in Soxhlet extractors for 16 hours, then repeatedly with triply-distilled water and filtered and dried as just described.

The actual starch content of each preparation was found by hydrolyzing with hydrochloric acid and determining the amount of glucose formed. The amount of 0 01 *N* acid or alkali required to render each starch preparation exactly neutral to rosolic acid was also determined. For each enzyme experiment so much of any given starch preparation was weighed out as would contain just sufficient actual starch to make the required amount of 1% substrate, and the small amount of 0.01 *N* acid or alkali required for strict neutrality to rosolic acid was added before bringing the starch dispersion to final volume or before mixing it with enzyme solution.

Enzyme Preparations.—The amylase preparations and other enzyme-containing materials used and the amount of each employed per 100 cc. of 1% starch dispersion were as follows: Pancreatic amylase preparation No. 64, 0.1 mg.; pancreatin No. 8, 2 5 mg.; fresh saliva, 0.18 to 0 5 cc.; malt extract, 0.15 cc.; malt amylase preparation No. 155, 0.25 mg.; amylase preparation No. 22 from *Aspergillus orysae*, 0 4 mg.; taka-diastase, 9.0 mg. Each enzyme was used in the presence of such amounts of chloride and phosphate as were believed to afford the most favorable conditions for its action.[1] Special precautions regarding preparation and use of triply distilled water, selection and care of glassware, avoidance of unnecessary exposure to light, etc., were observed as explained in previous papers from this laboratory dealing with other phases of our study of the amylases.

Method.—Amounts of the starch preparations sufficient in each case to furnish one gram of actual anhydrous starch were weighed out, mixed with a little cold water and gelatinized by pouring into boiling water and boiling for 3 minutes; then transferred to 100 cc. cylinders, neutralized, the necessary "activating" salts added and the mixtures brought to volume, thoroughly mixed by stirring and placed in a 40° thermostat water-bath. While the starch pastes thus prepared were reaching the temperature of the water bath, flasks containing uniform amounts of the enzyme were prepared. The substrate was then poured upon the enzyme, mixed thoroughly, and maintained for 30 minutes at 40°, both time and temperature being very strictly controlled. Finally the action of the enzyme was stopped by pouring into boiling water and quickly boiling the entire mixture, after which the reducing sugar which had been formed was determined volumetrically as explained above.

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[1] The influence of hydrogen ion concentration and of chlorides and phosphates has been discussed in several previous papers from this laboratory, THIS JOURNAL, 1910 to 1919.

Results.—The results of typical experiments comparing different starches, similarly purified, with each other (or in some cases differently purified portions of the same starches) are given in the tables which follow. On account of the nature of the enzyme solutions employed and the character of the manipulations involved in these experiments, only those data belonging to the same set of experiments—in general only the data in the same column of the same table—are directly comparable with each other in a quantitative sense.

Table I

Action of Saliva, Pancreatin, and Purified Pancreatic Amylase upon Water-washed, and upon Purified, Starches

Description of starch	% of starch hydrolyzed in 30 min. by		
	Saliva	Pancreatin	Pancreatic amylase Prep. No. 64
Water washed			
Wheat starch	56.8	32.2	42.8
Maize starch	50.6	25.1	31.6
Rice starch	61.5	36.1	45.8
Potato starch	67.7	39.7	47.2
Alkali washed			
Wheat starch			
(0.3% NaOH)	65.5	38.2	46.0
(0.15% NaOH)		38.4	
Maize starch			
(0.3% NaOH once)	66.3	38.3	46.7
(0.3% NaOH twice)		37.9	
Rice starch	65.7	38.3	46.4
Potato starch	67.0	39.4	34.0

The figures in any one column of Table I show that purification by washing with dil. alkali has a pronounced effect upon the comparison of the different starches with reference to their digestive hydrolysis. Potato starch is practically as pure and as accessible to saliva or pancreatin when merely washed with water as after purification by washing with dil. alkali, while water-washed maize "starch" contains impurities which markedly retard its digestion. To a less extent the same is true of wheat, while rice starch is almost as readily digested in the water-washed as in the alkali-washed condition. It is evident that the increased digestibility of the wheat and maize starches when purified by washing with dil. alkali is due to the removal of other material such as fatty or waxy matter, and not to predigestion of the starch itself by the alkali, since wheat starches treated with 0.15% and with 0.3% sodium hydroxide solutions are equally digestible and maize starch treated twice with the dil. alkali was not more digestible than that treated once. The low result obtained in the action of purified pancreatic amylase upon purified potato starch suggests the removal during purification of something essential to the optimum activation of the enzyme. This will be discussed in a later paper.

TABLE II

Action of Pancreatin and Purified Pancreatic Amylase upon Alkali-washed and upon Ether-washed Starches.

Description of starch	% of starch hydrolyzed in 30 min. by	
	Pancreatin	Pancreatic amylase. Prep No 64
Alkali-washed:		
Wheat starch	41.8	46.0
Maize starch	42.5	46.7
Rice starch	42.5	46.4
Potato starch	43.0	34.0
Ether-washed:		
Wheat starch	36.7	41.9
Maize starch	39.4	43.7
Rice starch	39.1	46.3
Potato starch	43.0	46.3

Examination of Tables II and III shows that the removal of fatty matter by ether tends to render the cereal starches more accessible to the enzymes as does purification with dil. alkali but not always to the same extent. Thus the low results obtained with water-washed maize starch might be attributed chiefly to fat which it contains, but the hydrolysis of rice starch by the purified aspergillus amylase is evidently retarded by material which is not removed by ether but is removed by washing with dil. alkali, as shown by comparison of Tables III and IV.

TABLE III.

Action of Different Enzymes upon Water-washed and upon Ether-washed Starches.

Description of starch	% of starch hydrolyzed in 30 min. by			
	Pancreatin	Pancreatic amylase Prep No. 64	Malt amylase Prep 155.	Aspergillus amylase. Prep. No. 22.
Water-washed:				
Wheat starch	40.4	39.1	38.3	42.5
Maize starch	29.1	27.3	36.8	31.5
Rice starch	40.5	42.4	39.6	15.2
Potato starch	44.9	43.8	42.2	42.9
Ether-washed:				
Wheat starch	43.5	39.7	38.6	42.6
Maize starch	44.3	41.8	39.0	39.9
Rice starch	44.0	44.0	39.8	21.9
Potato starch	44.6	44.0	42.2	40.1

TABLE IV.

Comparative Digestion of Different Starches when Purified by Washing with Dil. Alkali.

Kind of starch	% of starch hydrolysed in 30 min. by Saliva.	Pan-creatin.	Pancreatic amylase. Prep. No. 64.	Malt extract.	Malt amylase. Prep. 155.	Taka-diastase.	Aspergillus amylase. Prep. 22.
Wheat.........	40.2	38.2	41.8	54.5	34.5	48.2	37.8
Maize..........	40.6	38.9	42.4	54.8	35.6	44.7	39.7
Rice...........	41.5	38.9	42.1	54.5	35.4	48.3	39.7
Potato.........	43.5	39.4	29.0	56.8	35.2	52.4	38.2

TABLE V.

Comparative Digestion of Different Starches when Purified by Washing with Dil. Alkali and with Ether.

Kind of starch	% of starch hydrolyzed in 30 min. by Pan-creatin.	Pancreatic amylase Prep. 64.	Malt extract	Malt amylase Prep 155.	Taka-diastase.	Aspergillus amylase. Prep. 22.
Wheat................	40.7	39.0	53.1	38.7	43.5	39.8
Maize..................	41.0	39.8	52.3	39.1	42.7	39.5
Rice.........	41.5	39.8	53.3	39.4	43.2	39.5
Potato.................	44.4	27.7	55.4	40.7	46.0	42.2

Tables IV and V show that wheat, maize and rice starches, when similarly purified by washing with dil. alkali or alkali and ether, are of equal digestibility as measured by the method here used. This is true for each of the 3 typical amylases employed and regardless of whether the amylase was used in commercial or purified form. Except with purified pancreatic amylase[1] potato starch shows a digestibility or rate of enzymic hydrolysis equal to or slightly greater than that shown by the cereal starches. Thus with the single exception already noted, each column in Table V shows a slightly higher yield of maltose from potato starch than from the cereal starches tested (the variations among the latter being probably no greater than the possible error of experiment). In this connection it may be stated that preliminary results obtained in this laboratory by Dr. K. Hattori, in a study designed to compare the rate of hydrolysis of rice and potato starches by means of saliva throughout the course of digestion, have shown a slightly higher yield of reducing sugar from the potato than from the rice starch, the difference becoming perceptible when about 40% of the starch has been transformed to maltose and increasing gradually as the digestion is carried farther, probably because of a larger yield of relatively resistant dextrin from the rice, than from the potato, starch.

Conclusion.

When similarly purified by washing with very dil. alkali, wheat, maize and rice starches show the same digestibility in the sense that under the action of the same kind and amount of amylase they are all transformed into reducing sugar at essentially the same rate. This is true whether the digestive agent be saliva, pancreatin, purified pancreatic amylase, malt extract, purified malt amylase, taka-diastase, or the purified amylase of *Aspergillus oryzae*.

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[1] The abnormally low results in this single case will be discussed in a later paper.

As obtained by washing with water only, potato starch is almost pure, but the cereal starches appear to contain sufficient amounts of fatty or waxy matter to interfere to an appreciable extent with the action of the enzymes upon the starch even after the latter has been dispersed by boiling in water for 3 minutes. This was true to a greater extent of the maize than of the wheat starch, a finding in accordance with the results of natural digestion experiments[1] which emphasize the importance of such preparation of maize products as shall ensure their very thorough mastication and admixture with saliva.

Potato starch shows in general a rate of enzymic hydrolysis equal to or slightly greater than that of the cereal starches. As here tested, it is as readily acted upon in the water washed as in the more highly purified condition. The only case in which the potato starch has shown a distinctly lower rate of hydrolysis than that of the cereal starches, is one in which both starch and enzyme were employed in a highly purified condition. This tendency to abnormally low results is readily corrected by suitable additions to the digestion mixture as will be shown in a subsequent paper.

We are greatly indebted to the Carnegie Institution of Washington for grants in aid of this investigation.

NEW YORK, N Y

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF AMHERST COLLEGE.]

THE ACTION OF CUPROUS CHLORIDE WITH COMPOUNDS CONTAINING THE TRICHLOROMETHYL GROUP.

BY HOWARD WATERS DOUGHTY.

Received May 7, 1919.

In 1917 the present writer published a preliminary report[2] on the "Hydrolysis of Organic Halides and the Corrosion of Metals," in which it was shown that when compounds which contain the trihalogen-methyl group are brought in contact with copper in ammonia water, the copper goes into solution as ammono-cupric halide.

The facts that no evolution of gas is observed during the reaction, and that copper is oxidized to the cupric condition indicate that the reaction is not a simple hydrolysis, but that there is probably a condensation due to the presence of the ammonia, in which the heat of formation of the cupric halide as well as the "heat of ammonation" of the cupric ion play an important part. This feature will be dealt with more in detail in a subsequent contribution now in course of preparation.

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[1] Sherman and Winters, *J. Biol. Chem.*, 35, 301 (1918).

[2] THIS JOURNAL, 39, 2685 (1917).

In Experiment 15 of the previous contribution[1] it was shown that when a piece of copper foil is suspended in ammonia-water above and out of contact with carbon tetrachloride, the copper goes into solution very slowly, the solution around the copper remains colorless, and the solution at the zone of contact between the liquids acquires the deep blue color of the ammono-cupric ion. It was suggested that this behavior indicates that the course of the reaction involves solution of the copper as cuprous ion, with subsequent oxidation by the organic compound, which contains the trichloromethyl group. Bearing in mind the ease with which cuprous chloride is oxidized in ammoniacal solution, it appeared probable that cuprous chloride might be substituted for copper in the experiments previously recorded. If such should be the case it would afford a rapid and convenient means of demonstrating the presence of a trihalogen-methyl group in organic compounds provided the oxidation does not take place with compounds containing groups other than the trihalogen-methyl. The following experiments were performed to ascertain the applicability of this reaction as a test for the trichloro- and tribromo-methyl groups in organic compounds:

Procedure.—A few milligrams of the sample are placed in a small glass-stoppered bottle of 10 to 15 cc. capacity. (A test-tube with cork stopper can also be used.) The bottle is filled with conc. ammonia water. About 0.5 g. of powdered cuprous chloride is added and the stopper is quickly inserted, thus forcing out excess of liquid and excluding air. The bottle is shaken to dissolve the cuprous chloride. A blank test must be made for purposes of comparison.

In all cases in which a trichloro- or tribromo-methyl group was known to be present the deep blue color of the ammono-cupric ion developed within 5 minutes except in the case of hexachloro-ethane. In all other cases the development of color was much slower or failed entirely. The following table shows the results of the test as applied to various substances:

I. POSITIVE TEST WITHIN 5 MINUTES.

Substance.	Remarks.
Trichloro-acetic acid.	Instantaneous action.
Ethyl trichloro-acetate.	Dark blue in 2 minutes.
Chloral hydrate.	Dark blue in 2 minutes.
Dichloro-acetic acid.[2]	Dark blue in 3 minutes.

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[1] THIS JOURNAL, 39, 2688 (1917).

[2] The purity of the dichloro-acetic acid in respect to small amounts of trichloro-acetic acid or chloral is open to question. Very small amounts of either substance would account for this behavior.

Substance.	Remarks
Carbon tetrachloride.	Muddy, dark red solution, changing to dark blue in 2–3 minutes.
Chloroform.	Similar to carbon tetrachloride, but the red color is more persistent.
Bromoform.	No red color; green changing to dark blue in 5 minutes.
Chloropicrin.	Green, changing to dark blue in 2–3 minutes. Yellow precipitate.
Pentachloro-ethane.	Rapidly darkening blue color.
II. No Positive Test in 5 Minutes.	
Hexachloro-ethane.	Slight action at first, but dark blue at surface of contact after several hours. Crystals liquefy.
Iodoform.	Dark blue at surface of contact, but did not increase rapidly.
Monochloro-acetic acid.	No action.
Ethylidene chloride.	Cloudy amethyst color in 10 minutes.
Ethylene chloride.	No action
Ethylene bromide.	No action.
Ethyl bromide.	No action.
Butyl bromide.	No action.
Isobutyl bromide.	No action.
Benzyl chloride.	No action.
Trichloro-ethylene.	Slow action, dark in 24 hours.
Tetrachloro-ethylene.	Slow action, pale amethyst in 3 days.
Acetylene tetrachloride.	Slow action.
Nitrobenzene	Brown precipitate in 3 hours. No blue in solution.
m-Dinitrobenzene.	No color. Crystals changed to fluffy, white precipitate, filling tube.
Ammonium nitrate.	No action.
Collodion.	Very slow action at contact surface.
Smokeless powder.	Like collodion.
Benzaldehyde.	No action.
Benzenesulfonic acid.	No action.
Benzeneselenonic acid.	No acid.
Benzoyl peroxide	Slow action, marked after 4 hours.

From these experiments it is evident that this method can be used with considerable confidence in testing for the presence of the trichloro- or tribromo-methyl group in a compound, or even the detection of such compound in a mixture. The test is quickly made and requires only a very small amount of the substance; not much more than is needed for a determination of the melting point.

The study of this reaction is in progress in this laboratory, particularly as regards the action with the chloro-acetic acids.

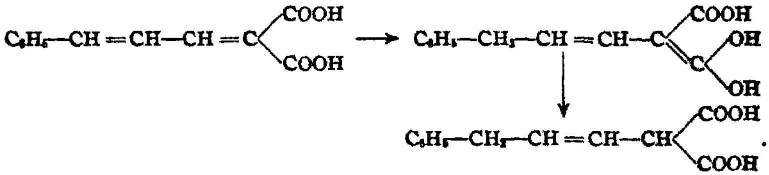
Amherst, Mass.

SOME FACTORS BEARING UPON 1,6-ADDITION.[1]

By Tenney L. Davis.

Received May 7, 1919.

That 1,6-addition sometimes takes place has been demonstrated by Straus,[2] who showed that, in the dichloride which is formed when cinnamylidene-acetophenone is treated with phosphorus pentachloride, the two chlorine atoms are in the 1,6-positions with reference to one another. Cinnamylidene-malonic acid when treated with sodium amalgam takes up two hydrogen atoms, and the compound which is formed has been shown by Riiber[3] to be 1,4-hydrocinnamylidene-malonic acid. Its formation is probably due to primary addition of hydrogen in the 1,6-positions and subsequent rearrangement of the product—just as the reduction of cinnamic acid under similar conditions is probably due to 1,4-addition.



$$C_6H_5-CH=CH-CH=C\begin{matrix}COOH\\COOH\end{matrix} \longrightarrow C_6H_5-CH_2-CH=CH-C\begin{matrix}COOH\\ \| \\ C\begin{matrix}OH\\OH\end{matrix}\end{matrix}$$

$$\downarrow$$

$$C_6H_5-CH_2-CH=CH-CH\begin{matrix}COOH\\COOH\end{matrix}.$$

The interesting question arises whether 1,6-addition will take place in a similar manner with a substance which lacks the middle one of the 3 unsaturated linkages that go to make up the 1,6-conjugated system.

The 1,4-hydrocinnamylidene-malonic acid, which is the immediate product of the reduction, has been shown by Riiber to undergo slow rearrangement into the 3,4-compound, which is evidently more stable. Moreover, Hinrichsen and Triepel[4] found that the primary addition product of bromine and cinnamylidene-malonic ester is the 3,4-compound—in the case where 1,6- or 1,4-addition with the carbonyl group involved was impossible or altogether unlikely, with bromine.

Thiele and Meisenheimer have found that hydrocyanic acid adds to cinnamylidene-malonic ester in the α,β-positions instead of in the α,δ-positions as they expected.[5] This addition, however, is probably not 1,2-addition to the unsaturated linkage, but, in view of the comportment of this compound with the Grignard reagent, is probably 1,4-addition where the carbonyl group is involved.

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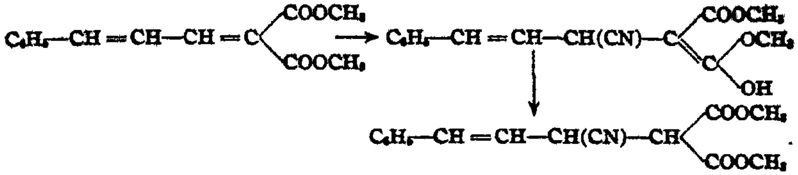
[1] An abstract of part of a thesis submitted to the Division of Chemistry of Harvard University in fulfilment of the requirements for the degree of Doctor of Philosophy, June 1917. The research was suggested by Professor Elmer P. Kohler and was carried out at the University of California where I was a guest. Grateful acknowledgment is hereby made to Prof. Kohler for helpful advice and to the University of California for laboratory facilities.—T. L. D.

[2] Straus, *Ann.*, 370, 315 (1909).

[3] Riiber, *Ber.*, 35, 2311 (1902).

[4] Hinrichsen and Triepel, *Ann.*, 335, 196 (1904).

[5] Thiele and Meisenheimer, *Ibid.*, 306, 247 (1899).



$$C_6H_5{-}CH{=}CH{-}CH{=}C\begin{cases}COOCH_3\\COOCH_3\end{cases} \longrightarrow C_6H_5{-}CH{=}CH{-}CH(CN){-}C\begin{cases}COOCH_3\\ {=}C\begin{cases}OCH_3\\OH\end{cases}\end{cases}$$

$$\downarrow$$

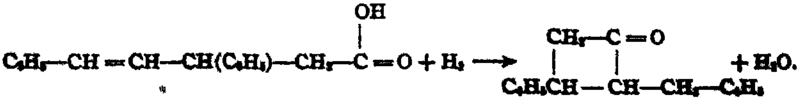
$$C_6H_5{-}CH{=}CH{-}CH(CN){-}CH\begin{cases}COOCH_3\\COOCH_3\end{cases}.$$

E. P. Kohler and Miss Marie Reimer[1] and their co-workers have found that cinnamylidenemalonic ester, α-methyl and α-cyan-cinnamylideneacetic ester, and other analogous compounds which contain a 1,6-conjugated system, combine with the Grignard reagent in the 1,4-positions, the 5,6-unsaturated linkage being unaffected. They also react 1,2-, the carbonyl group being involved and the alkoxyl group being replaced by the hydrocarbon residue which is in combination with the magnesium, the relative amounts of 1,2- and of 1,4-addition depending in these cases upon the relative rates at which the Grignard reagent combines with the 1,2- and with the 1,4-systems.

It seemed of interest to examine by experiment whether 1,6-addition could be made to take place in a compound in which the possibility of 1,4-addition was eliminated by the lack of the unsaturated linkage in the 3,4-position.

Barbier[2] experimented with one such compound. By allowing natural methyl-heptenone to react with methyl iodide in the presence of metallic magnesium, he obtained 2,6-dimethyl-heptene-2 ol-6, indicating that with that substance only the carbonyl group is involved when it reacts with methylmagnesium iodide.

In the present investigation 2,4-diphenyl-butene-3 acid-1 was synthesized. This substance differs from similar substances which have been found to enter into 1,6-addition reactions by the lack of an unsaturated linkage in the 3,4-position; and, if it were to combine 1,6- with hydrogen, the carbon atoms occupying the 2- and 5-positions would become linked directly to one another, and the resulting cyclobutane derivative, having two hydroxyl groups on the same carbon atom, would lose water to form a ketone—which could be easily identified by its properties.



$$C_6H_5{-}CH{=}CH{-}CH(C_6H_5){-}CH_2{-}\overset{\displaystyle OH}{\overset{|}{C}}{=}O + H_2 \longrightarrow \begin{matrix} & CH_2{-}C{=}O \\ & |\qquad\ | \\ C_6H_5CH & {-}\,CH{-}CH_2{-}C_6H_5 \end{matrix} + H_2O.$$

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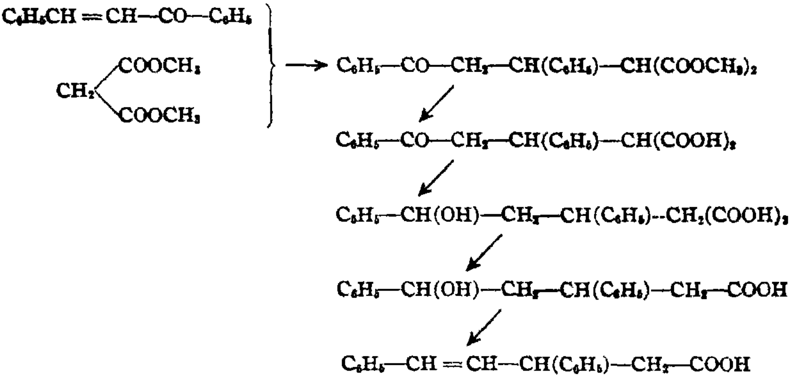
[1] Kohler and Reimer, *Am. Chem. J.*, 33, 333 (1905); Reimer, *Ibid.*, 38, 227 (1907); Reimer and Reynolds, *Ibid.*, 40, 428 (1908); 48, 206 (1912); Reynolds, *Ibid.*, 46, 198 (1911).

[2] Barbier, *Compt. rend.*, 128, 110 (1899).

It was found, however, that the acid is not reduced when boiled with zinc dust and acetic acid, or when its sodium salt in aqueous solution was treated with sodium amalgam. It reacts with phenyl-magnesium bromide to form an unsaturated tertiary alcohol. This substance, therefore, in its comportment toward nascent hydrogen and toward the Grignard reagent, reacts differently from substances similar to it but differing from it by having an unsaturated linkage in the α,β-position, its γ,δ-unsaturated linkage not being affected by either of these reagents; and the results indicate that a 3,4-unsaturated linkage is somehow a necessary factor for the accomplishment of 1,6-addition.

Experimental Part.

2,4-Diphenyl-butene-3 acid-1 was prepared by hydrolyzing the addition product of malonic ester and benzal-acetophenone, by reducing the δ-ketonic acid so obtained, and by splitting off water and carbon dioxide from the resulting hydroxy acid.



$$\left.\begin{array}{l} C_6H_5CH=CH-CO-C_6H_5 \\ CH_2(COOCH_3)_2 \end{array}\right\} \longrightarrow C_6H_5-CO-CH_2-CH(C_6H_5)-CH(COOCH_3)_2$$

$$C_6H_5-CO-CH_2-CH(C_6H_5)-CH(COOH)_2$$

$$C_6H_5-CH(OH)-CH_2-CH(C_6H_5)-CH_2(COOH)_2$$

$$C_6H_5-CH(OH)-CH_2-CH(C_6H_5)-CH_2-COOH$$

$$C_6H_5-CH=CH-CH(C_6H_5)-CH_2-COOH$$

Benzal-acetophenone was condensed with methyl and with ethyl malonate by the method recommended by Kohler.[1] The ketone was boiled under reflux for half an hour with about its own weight of absolute alcohol, slightly more than one equivalent of malonic ester, and enough sodium alcoholate to give the solution an alkaline reaction to litmus. The mixture was cooled at once at the tap, and seeded. The crystals which separated were filtered off and washed, and a second crop of crystals was obtained from the mixture after it had been allowed to stand overnight. The yields were good—about 80% of the calculated quantity.

The 2,4-diphenyl-butanone-4 diacid-1,1 methyl or ethyl ester hydrolyzes readily. It was dissolved in warm alcohol and twice the equivalent quantity of potassium hydroxide in a small quantity of water was added while the mixture was shaken. When the alkali was added, the colorless solution instantly took on a yellow or orange color, and, after a moment's shaking, set to a stiff, pasty mass of crystals. It was allowed to stand for two days, at the end of which time the white needle crystals were filtered off and washed thoroughly, first with alcohol and then with ether. The product so obtained dissolved readily in water to yield a clear, colorless solution. During the hydrolysis some of the substance reverted to benzalacetophenone, thus reducing somewhat the yield of the potassium salt. In general, the weight of the potassium salt which was obtained was greater than that of ester which was used: the best yield was 270 g. of potassium salt from 200 g. of ethyl ester.

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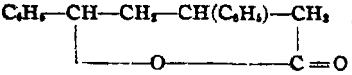
[1] Kohler, *Am. Chem. J.*, 46, 474 (1911).

The reduction of the ketonic acid yielded an acid reaction product which was very soluble in ether. The ether deposited crystals which were so soluble in ether that they could not be washed on the filter. The mother-liquors were viscous and difficult to handle. They finally set to a pasty mass of very small crystals, and this at length dried to a white, brittle, powdery mass. This white, brittle mass was worked up directly with acetic anhydride, for it was found that this part of the synthesis went smoothly and that good yields of the unsaturated acid were obtained.

Reduction of the δ-Ketonic Acid.—In one experiment 103 g. of the potassium salt was dissolved in a liter of water in a tall, glass cylinder and a large excess of sodium amalgam—21 g. of sodium in 900 g. of mercury—was thrown in. After 4 days, when the reaction appeared to be over, the solution was iced, made acid with hydrochloric acid, and shaken out with ether. The material deposited from the ether could not be manipulated and it finally yielded a crystal mush weighing 77 g. This was taken up in a hot mixture of benzene with a little methyl alcohol, and subjected to a systematic fractional crystallization. There was obtained 2 g. of a pure substance which was evidently—

β,δ-Diphenyl-δ-hydroxy-butyric Acid Lactone,



$$\begin{array}{l} C_6H_5\text{—}CH\text{—}CH_2\text{—}CH(C_6H_5)\text{—}CH_2 \\ \quad\;\;\, |\qquad\qquad\qquad\qquad\quad\;\; | \\ \quad\;\;\, \text{———}O\text{—————}C=O \end{array}$$

.—It crystallizes from ethyl alcohol in beautiful, transparent, colorless needles, melting at 113–114° without decomposition. The crystals are not soluble in sodium carbonate solution either hot or cold. Their solution in alcohol gives a marked yellow color with one drop of ferric chloride solution—a much deeper color then results when one drop of ferric chloride is added to the same amount of pure alcohol. Half a gram of the substance boiled for half an hour with about 5 times its weight of acetic anhydride was recovered unchanged when the acetic anhydride was poured into water, the water shaken out with ether, and the ether allowed to evaporate. The substance dissolves in wet alcoholic potash and there is no precipitate when the alcoholic solution is diluted with a large quantity of water; but, if this solution is made acid and extracted with ether, the ether deposits the original substance. These are the properties of a lactone.

Calc. for $C_{17}H_{16}O_2$: C, 80.95; H, 6.347. Found: C, 80.89; H, 6.518.

The properties of the substance and its composition indicate that it is the δ-lactone.

The conjunction of the two facts, that the substance was not altered by boiling with acetic anhydride, and that it did not appear in the product of any of the experiments in which the crude product of the reduction was boiled with acetic anhydride, indicates that it was probably formed, not as an intermediate product of the reduction, but because of the manner in which the reduction product was handled.

In another reduction experiment 270 g. of the potassium salt was treated, as before, with sodium amalgam consisting of 21 g. of sodium and 900 g. of mercury After 4 days the aqueous solution was iced and acidified with hydrochloric acid. An oil separated. The sides of the container were scratched with a glass rod, and the next morning it was found that the oil has solidified to a mass of crystals These, washed with water and dried, melted at 114–117° with decomposition. By fractional crystallization from benzene with a little methyl alcohol, and by extraction of the lower melting fractions with hot water, two substances were isolated—(*a*) the hydroxy-malonic acid derivative which constituted perhaps 3% of the reaction product, and (*b*) β,δ-diphenyl-δ-hydroxy-butyric acid which made up the large part of the reaction product.

2,4-Diphenyl, 4-Hydroxy-butane, Diacid-1,1 crystallizes from warm water, in which it is fairly soluble, in wart-like masses of colorless, radiating, stout needles which melt at 190–195° and turn brown and give off gas at the melting point. It is readily soluble in sodium carbonate solution from which it liberates gas.

Calc. for $C_{18}H_{18}O_5.2H_2O$: C, 61.72; H, 6.285. Calc. for $C_{18}H_{18}O_5.3H_2O$: C, 58.65 H, 6.570. Found: C, 60.64, 59.96; H, 5.572, 4.831.

The properties of the substances are in accord with the belief that it is a malonic acid derivative. It seems probable therefore that it is 2,4-diphenyl, 4-hydroxy-butane diacid-1,1 which had crystallized with two molecules of water and which had decomposed slightly, losing some carbon dioxide and some of its water.

β,δ-Diphenyl-δ-hydroxy-butyric Acid is but little soluble even in hot water. It dissolves readily in sodium carbonate solution. It crystallizes, with half a molecule of water of crystallization, in colorless needles from benzene and in pearly flakes from alcohol, and melts at 154–154.5° with the evolution of gas but without the production of any color.

Calc. for $2[C_{17}H_{18}O_3]\,H_2O$: C, 73.10; H, 6.861. Found: C, 73.08; H, 6.603.

The structure of this acid is demonstrated by its properties and composition, and by the fact that it yields the desired unsaturated acid when it is boiled with acetic anhydride.

Elimination of Water from the Reduced Acid.—Since it was found that the principal product of the reduction is a substance that yields the desired unsaturated acid when it is boiled with acetic anhydride, and since it was found that the unsaturated acid is much easier to isolate from its reaction mixture than the corresponding hydroxy-acid, it was found expedient to treat the crude product of the reduction at once with acetic anhydride without previous purification. The yields were fair. Two typical experiments are described.

18 g. of the white, brittle crude reduced acid was boiled for an hour with 50 cc. of acetic anhydride to which 8 drops of conc. sulfuric acid had been added. The mixture was poured into ice-water. An oil separated. After standing overnight, the oil had become a sticky solid. This was washed in water and dried in a vacuum desiccator—yielding 18.8 g. of a brown putty-like mass which smelled strongly of acetic acid. This was taken up in hot benzene and the solution yielded crystals from which, after several crystallizations, 9.6 g. of the pure unsaturated acid was obtained. The residue was a tar from which nothing further could be isolated.

82 g. of the crude reduced acid was boiled for an hour with 200 cc. of acetic anhydride to which about one cc. of conc. sulfuric acid had been added. The mixture was poured into water and allowed to stand for two days. The black, putty-like mass which resulted was recrystallized from benzene, yielding 23.6 g. of the pure unsaturated acid.

2,4-Diphenyl-butene-3 Acid-1 crystallizes from benzene in colorless, rhomb-shaped needles, m. p. 124–125°. It is somewhat soluble in hot water, from which it is deposited, when the solution cools, in transparent needles. It dissolves readily in aqueous sodium carbonate solution, and the solution discharges the color of permanganate instantly.

Calc. for $C_{17}H_{16}O_2$: C, 80.95; H, 6.34. Found. C, 80.00, 80.96; H, 6.421, 6.404.

Molecular-weight determinations by measurement of the freezing points of benzene solutions gave the figures 537.9 and 439.0.

Calc. for $(C_{17}H_{16}O_2)_2$: 504.

It appears therefore that the acid exists in benzene solution in the form of a double molecule. The structure of the acid is demonstrated by the fact that it yields benzoic acid and phenyl-succinic acid on oxidation.

$$C_6H_5—CH = CH—CH(C_6H_5)—CH_2—COOH + 4[O] \longrightarrow$$
$$C_6H_5—COOH + C_6H_5—CH(COOH)—CH_2—COOH.$$

When a boiling aqueous solution of the sodium salt was oxidized with potassium permanganate, the odor of benzaldehyde appeared, and, later, the odor of benzoic acid. Nothing but benzoic acid could be isolated from the reaction product. When the oxidation was carried out in an iced solution, the manganese dioxide dissolved by the addition of sulfurous acid, the solution made acid and shaken out with ether, the ether deposited an oil which smelt strongly of benzaldehyde. After standing for a few weeks in the laboratory, the oil showed the presence of crystals; the odor of benzaldehyde had disappeared and an odor of aliphatic aldehydes remained. At the end of 8 weeks, the mass had crystallized in large part. By fractional crystallization and by extraction of the higher melting fraction with chloroform, the material was divided into benzoic acid and phenyl-succinic acid, which were identified by their melting points.

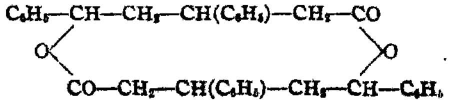
2,4-Diphenyl-butene-3 Acid-1 Methyl Ester.—The methyl ester first obtained by the action of methyl iodide in ether solution on the silver salt of the acid proved to be an oil, and the usual expedients—such as scratching with a glass rod, leaving in a vacuum desiccator, or freezing the methyl alcohol solution with liquid air—failed, to make it crystallize. A few drops, however, in the bottom of a beaker finally crystallized in white needles after a month's standing in the corner of the laboratory. With this *seed* at hand, the preparation of a larger amount was carried out successfully. The ester crystallizes from methyl alcohol in beautiful, radiating clusters of thick, transparent needles, m. p. 47–8°. In acetone solution it discharges the color of permanganate instantly.

Calc. for $C_{18}H_{18}O_2$: C, 81.21; H, 6.766. Found: C, 81.16; H, 7.423.

β,δ-Diphenyl-δ-hydroxy-butyric Acid Self Ester was obtained as a by-product in one preparation of the unsaturated acid, and in one only. The experiment in which this substance was obtained differed, so far as I know in no essential respect from similar experiments in which none of the substance appeared. 31 g. of the crude reduction product of the ketonic acid was boiled for half an hour with 100 g. of acetic anhydride to which 8 drops of conc. sulfuric acid had been added, the mixture was treated with water, and shaken out with ether. The ether deposited crystals which yielded, on recrystallization from benzene, 8 g. of a pure substance which crystallized from benzene in colorless, transparent needles, m. p. 92–94°. The substance is not soluble in sodium carbonate solution and, when warmed with a strong solution, it melts but does not dissolve. Its solution in acetone reduced permanganate rapidly but not instantly.

Calc. for $C_{34}H_{32}O_4$: C, 80.95; H, 6.347. Found: C, 81.17, 81.36; H, 6.066, 5.987.

The analysis is in good agreement with the belief that this substance is the "self ester" of β,δ-diphenyl, δ-hydroxy-butyric acid, formed from that acid by the combination of two molecules and the consequent elimination of two molecules of water.



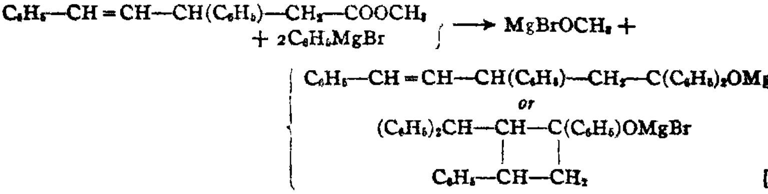
This hypothesis was verified by experiment. A quantity of the substance was dissolved in wet alcoholic potash and the solution was allowed to stand for 3 days. On diluting it with a large quantity of water, there was no precipitate. The solution was made acid and shaken out with ether. The ether deposited the expected acid in a state of purity.

Attempts to Reduce the Unsaturated Acid.—3 g. of 2,4-diphenylbutene-3 acid-1 was dissolved in aqueous sodium carbonate solution in a 50 cc. graduate, and sodium amalgam, consisting of one g. of sodium and 50 g. of mercury, was thrown in. After several days, when the evolution of gas had ceased, the solution was acidified and shaken out with ether. From the ether only the original acid and no other substance was obtained.

A repetition of the experiment gave the same result.

5 g. of the acid, 30 g. of zinc dust, 60 cc. of glacial acetic acid, and 5 cc. of water were boiled together under reflux for two hours. The mixture was treated with water and ether, and the ether proved to contain only the original acid and no other substance The unsaturated acid, therefore, is not reduced under these conditions.

Reaction of the Methyl Ester with Phenyl Magnesium Bromide.—The methyl ester reacts in dry ether with two equivalents of phenyl-magnesium bromide Immediately upon mixing the substances, there is a white precipitate, and indeed the entire appearance of the reaction is similar to that of the reaction of ethyl benzoate and phenyl-magnesium bromide. Two reactions are possible



$$\left.\begin{array}{l} C_6H_5—CH=CH—CH(C_6H_5)—CH_2—COOCH_3 \\ \qquad + 2C_6H_5MgBr \end{array}\right\} \longrightarrow MgBrOCH_3 +$$

$$\left\{\begin{array}{lr} C_6H_5—CH=CH—CH(C_6H_5)—CH_2—C(C_6H_5)_2OMgBr & \\ \qquad or & [I] \\ (C_6H_5)_2CH—\underset{\displaystyle C_6H_5—CH}{\underset{|}{CH}}—\underset{\displaystyle CH_2}{\underset{|}{C}}(C_6H_5)OMgBr & [II] \end{array}\right.$$

The product, which is obtained in a state of purity when the reaction mixture is treated with water, reduces permanganate in acetone solution indicating that the reaction is in accord with the first of the two equations above and that the γ,δ-unsaturated ester does not react in the 1,6-positions with the Grignard reagent under these conditions.

The product of the Grignard reaction consisted of only one substance, crystallizing from hot alcohol, in which it was not very soluble, in beautiful, colorless, thin needles, m. p. 138–139°. A solution of the substance in acetone discharges the color of permanganate instantly. It dissolves in conc. sulfuric acid to yield an orange-colored solution.

Calc. for $C_{29}H_{26}O$: C, 89.23, H, 6.667. Calc. for $C_{29}H_{25}OC_{29}H_{25}$: C, 91.36; H, 6.561. Found: C, 88.82, 89.45; H, 7.506, 7.05.

The analysis indicates that the substance which was isolated is the carbinol and not the corresponding ether. When a gram of the carbinol was boiled for half an hour with acetic anhydride and the reaction mixture was poured into alcohol, the original substance was recovered unchanged. It, therefore, does not form a stable acetate under these conditions. This fact, however, is quite in harmony with the conduct of other tertiary alcohols of this type.

SOMERVILLE, MASS

[CONTRIBUTION FROM THE CARBOHYDRATE LABORATORY, BUREAU OF CHEMISTRY, UNITED STATES DEPARTMENT OF AGRICULTURE.]

THE AMIDE OF α-*d*-MANNOHEPTONIC ACID.

BY C. S. HUDSON AND K. P. MONROE.

Received May 15, 1919

This substance was first noted by Fischer[1] as a precipitate settling from the reaction mixture of hydrogen cyanide and *d*-mannose in aqueous solution. He identified the substance as an amide by its behavior towards alkalies and iron salts, found its m. p. to be 182–3°, but published no analysis or record of its purification. Its specific rotation was not measured. As we desired to know its rotatory power we prepared it in similar manner but soon reached the conclusion that it was by no means a pure compound because on successive recrystallizations its m. p. rose to 193–4° and its specific rotation increased from +4 to +28°. These higher values were found only after the substance had been recrystallized 6 times but further recrystallization did not change them. As the substance was difficult to purify and there seeemed a possibility of the presence in it of the isomeric β-*d*-mannoheptonic amide, or some other impurity, a second method for preparing it was studied. Ten g. of pure crystalline α-*d*-mannoheptonic lactone was dissolved in 100 cc. of 50% alcohol, the solution was cooled with ice and ammonia was passed into it to saturation. A fine, white, granular precipitate formed, which was filtered off and washed with cold 50% alcohol. Its m. p. was 184–5° and $[\alpha]^{20}_{D} = +14$. After only two recrystallizations from hot water its m. p. was 193–4° and $[\alpha]^{20}_{D} = +27.8°$, both of which agree with the values found for the other preparation of this amide.

The purified amide from the hydrogen cyanide reaction was found to contain 6.1% and 5.9% N in two analyses by the Kjeldahl method, which agree with the theoretical value for $CH_2OH.CHOH.CHOH.CHOH.CHOH.CHOH.CONH_2$, 6.2%. The purified amide made by the action f ammonia on the lactone gave 5.9% and 6.1% N. An aqueous solution of the purified amide from the HCN reaction, containing 0.542 g. substance in 50 cc. solution rotated 1.21° to the right at 20° in a 4 dcm. tube with sodium light; hence $[\alpha]_D^{20} = +28.0$. A second measurement gave $+28.1$. A solution of the purified amide that had been made from the lactone, containing 0.405 g. in 50 cc. solution, rotated 0.90° to the right at 20° in a 4 dcm. tube with sodium light; hence $[\alpha]_D^{20} = +27.8$. The average of the 3 measurements, $+28.0$, is taken as the specific rotation of the pure amide.

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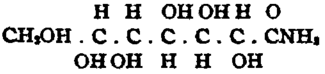
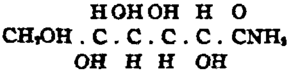
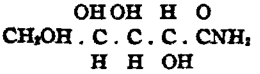
[1] *Untersuchungen über Kohlenhydrate und Fermente*, p. 300.

It is interesting to observe that the molecular rotations of the amides of *α-d*-mannoheptonic, *d*-galactonic and *l*-arabonic acids have the same sign and nearly the same numerical values.

TABLE I.

Rotation of Three Amides of Similar Terminal Configuration.

Amide.	Configuration	Specific rotation	Molecular[1] rotation
α-d-Mannoheptonic....	 $CH_2OH.\underset{OH}{\overset{H}{C}}.\underset{OH}{\overset{H}{C}}.\underset{H}{\overset{OH}{C}}.\underset{H}{\overset{OH}{C}}.\underset{OH}{\overset{H}{C}}.\overset{O}{C}NH_2$	+28.0	$+63.0(10)^2$
d-Galactonic.....	 $CH_2OH.\underset{OH}{\overset{H}{C}}.\underset{H}{\overset{OH}{C}}.\underset{H}{\overset{OH}{C}}.\underset{OH}{\overset{H}{C}}.\overset{O}{C}NH_2$	+30.2	$+58.9(10)^2$
l-Arabonic...... ...	 $CH_2OH.\underset{H}{\overset{OH}{C}}.\underset{H}{\overset{OH}{C}}.\underset{OH}{\overset{H}{C}}.\overset{O}{C}NH_2$	+37.9	$+62.5(10)^2$

The cause of this agreement evidently lies in the fact that the three structures have the same configurations for the α-, β- and γ-carbon atoms near the amide groups. In an accompanying article by Hudson and Komatsu it is shown that the principle of optical superposition holds fairly closely for such amides as these and that the α- and β-carbon atoms are the only ones that have much influence on the rotation

WASHINGTON, D C

[CONTRIBUTION FROM THE CARBOHYDRATE LABORATORY, BUREAU OF CHEMISTRY UNITED STATES DEPARTMENT OF AGRICULTURE.]

THE ROTATORY POWERS OF THE AMIDES OF SEVERAL α-HYDROXY ACIDS OF THE SUGAR GROUP.

BY C. S. HUDSON AND SHIGERU KOMATSU.

Received May 15, 1919

In a recent article[2] it was shown that Weerman's measurements of the rotatory powers of the amides of 7 α-hydroxy acids of the sugar group lead to the generalization that the α-carbon atom is principally responsible for the rotation of these substances and that *when the hydroxyl group is on the right of this carbon atom, in the configurations of Fischer's, the amide rotates to the right and vice versa.* This conclusion was borne out further by the known configurations and rotations of tartraminic acid, tartramide and the amides of malic and glyceric acids. By its application to the amide of mandelic acid the configurations of the active forms of this acid were placed in the system that Fischer originated for the sugar group, which will doubtless in time grow to include most optically active substances. In that article it was stated that Weerman's measurements seemed to lack the precision that would be required in a quantitative study of the rotations of the other active carbon atoms of the amides of the sugar acids. At present we wish to treat this subject quantitatively, basing the study upon measurements that one of us (S. K.) has made during the past year. These measurements confirm the generalization already mentioned, but they differ in some instances from Weerman's data and lead to some interesting conclusions that are not apparent from his measurements.

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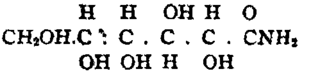
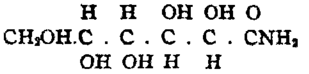
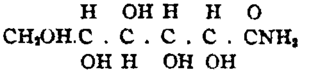
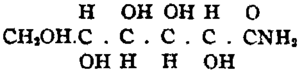
[1] The molecular weights of the 3 amides are 225, 195 and 165.

[2] THIS JOURNAL, 40, 813 (1918).

Consider first the molecular rotations (m. w. 195) in aqueous solution of the amides of the group of acids that are related to the hexoses, the so-called hexonic acids, namely, gluconic, mannonic, gulonic and galactonic acids.

Table I.—Configurations and Rotations of Hexonic Amides.

Amide	Fischer's configuration	Specific rotation	Molecular rotation.
d-Gluconic amide.......	 $\mathrm{CH_2OH.}\overset{\mathrm{H}}{\underset{\mathrm{OH}}{\mathrm{C}}}\,.\,\overset{\mathrm{H}}{\underset{\mathrm{OH}}{\mathrm{C}}}\,.\,\overset{\mathrm{OH}}{\underset{\mathrm{H}}{\mathrm{C}}}\,.\,\overset{\mathrm{H}}{\underset{\mathrm{OH}}{\mathrm{C}}}\,.\,\overset{\mathrm{O}}{\mathrm{C}}\mathrm{NH_2}$	$+31.2$	$+60.8(10)^2$
d-Mannonic amide......	 $\mathrm{CH_2OH.}\overset{\mathrm{H}}{\underset{\mathrm{OH}}{\mathrm{C}}}\,.\,\overset{\mathrm{H}}{\underset{\mathrm{OH}}{\mathrm{C}}}\,.\,\overset{\mathrm{OH}}{\underset{\mathrm{H}}{\mathrm{C}}}\,.\,\overset{\mathrm{OH}}{\underset{\mathrm{H}}{\mathrm{C}}}\,.\,\overset{\mathrm{O}}{\mathrm{C}}\mathrm{NH_2}$	-17.3	$-33.7(10)^2$
d-Gulonic amide.........	 $\mathrm{CH_2OH.}\overset{\mathrm{H}}{\underset{\mathrm{OH}}{\mathrm{C}}}\,.\,\overset{\mathrm{OH}}{\underset{\mathrm{H}}{\mathrm{C}}}\,.\,\overset{\mathrm{H}}{\underset{\mathrm{OH}}{\mathrm{C}}}\,.\,\overset{\mathrm{H}}{\underset{\mathrm{OH}}{\mathrm{C}}}\,.\,\overset{\mathrm{O}}{\mathrm{C}}\mathrm{NH_2}$	$+15.2$	$+29.6(10)^2$
d-Galactonic amide......	 $\mathrm{CH_2OH.}\overset{\mathrm{H}}{\underset{\mathrm{OH}}{\mathrm{C}}}\,.\,\overset{\mathrm{OH}}{\underset{\mathrm{H}}{\mathrm{C}}}\,.\,\overset{\mathrm{OH}}{\underset{\mathrm{H}}{\mathrm{C}}}\,.\,\overset{\mathrm{H}}{\underset{\mathrm{OH}}{\mathrm{C}}}\,.\,\overset{\mathrm{O}}{\mathrm{C}}\mathrm{NH_2}$	$+30.2$	$+58.9(10)^2$

Since there are 4 asymmetric carbon atoms in these structures the rotation of each of them can be calculated from the rotations of the 4 amides on the assumption of the principle of optical superposition. The details of the method of calculation have already been published.[1] It is found in this way that the molecular rotations for the 4 carbon atoms, calling the active atom next the amide end the α-carbon, have the following values when the hydroxyl group is on the lower side of its carbon atom (or is on its right when the formula is written vertically with the amide group at the top): α-carbon $= +47.25(10)^2$, β-carbon $= -14.65(10)^2$,

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[1] This Journal, 39, 465 (1917).

γ-carbon = $+0.95(10)^2$, and δ-carbon = $-2.05(10)^2$. It will be noticed that the numerical values decrease as the carbon atom is further removed from the amide end (the difference between the values for the γ- and δ-atoms, both of which are very small, are probably near the limit of accuracy of the data). The alternation in the sign of the rotation of the successive carbon atoms is also noteworthy, suggesting the alternation in positive and negative affinity that is often ascribed to the carbons in a chain.

Consider next the amides of several of the acids of the heptose group.

TABLE II.—CONFIGURATIONS AND ROTATIONS OF HEPTONIC AMIDES.

Amide.	Fischer's configuration	Specific rotation	Molecular rotation (Mol wt 225)
α-Glucoheptonic..	H H OH H H O $CH_2OH.C . C . C . C . C . CNH_2$ OH OH H OH OH	+10.6	$+23.8(10)^2$
β-Glucoheptonic	H H OH H OH O $CH_2OH.C . C . C . C . C . CNH_2$ OH OH H OH H	—30.2	$-67.9(10)^2$
α-Mannoheptonic[1]......	H H OH OH H O $CH_2OH.C . C . C . C . C . CNH_2$ OH OH H H OH	+28.0	$+63.0(10)^2$
α-Galaheptonic..... ..	H OH OH H H O $CH_2OH.C . C C . C . C . CNH_2$ OH H H OH OH	+14.3	$+32.2(10)^2$

Although it is not possible to calculate the rotations of all 5 of the active carbon atoms in these chains, because only 4 observations are at hand, nevertheless the following molecular rotations may be determined: α-carbon = $+45.85(10)^2$, β-carbon = $-19.6(10)^2$, δ-carbon = $-4.2(10)^2$, ϵ-carbon — γ-carbon = $+1.75(10)^2$. It is noticeable again that the sign alternates from carbon to carbon. The numerical value for the α-carbon is almost the same as was found for the hexonic amides, showing that the principle of optical superposition holds at least closely in passing from one of these groups to the other. Also the values for the other carbons correspond very well within the two groups. It seems highly probable, therefore, that the principle holds closely among the members of each group. One could, of course, calculate with fair approximation the rotation of the amides of several of the hexonic and heptonic acid amides that have not yet been measured, such as allonic amide or guloheptonic amide, but the mention of this may suffice at present.

Consider next the amides of the pentonic acids.

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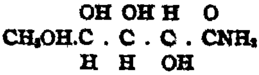
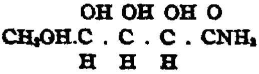
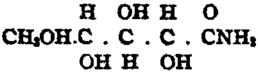
[1] The rotation of this substance is quoted from the accompanying article by Hudson and Monroe.

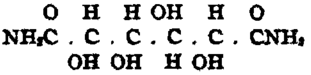
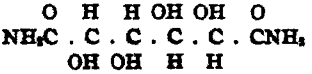
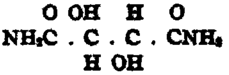
TABLE III.—CONFIGURATIONS AND ROTATIONS OF PENTONIC AMIDES.

Amide.	Fischer's configuration.	Specific rotation.	Molecular rotation. (Mol. wt. 165.)
l-Arabonic amide............	 $CH_2OH.\underset{H}{\overset{OH}{C}}.\underset{H}{\overset{OH}{C}}.\underset{OH}{\overset{H}{C}}.\overset{O}{C}NH_2$	+37.5	+61.9(10)^2
l-Ribonic amide.............	 $CH_2OH.\underset{H}{\overset{OH}{C}}.\underset{H}{\overset{OH}{C}}.\underset{H}{\overset{OH}{C}}.\overset{O}{C}NH_2$	—16.4	—27.1(10)^2
d-Xylonic amide............	 $CH_2OH.\underset{OH}{\overset{H}{C}}.\underset{H}{\overset{OH}{C}}.\underset{OH}{\overset{H}{C}}.\overset{O}{C}NH_2$	+44.5	+73.4(10)^2

From these 3 values the molecular rotations of the 3 active carbon atoms in the pentonic amides may be calculated to be, α-carbon = +44.5(10)^2, β-carbon = —23.15(10)^2, γ-carbon = +5.75(10)^2. The value for *d*-xylonic amide is taken from Weerman's article, as we have not been able to crystallize this substance. The value for the α-carbon is obtained by the use only of our own data for the amides of arabonic and ribonic acids, both of which have been prepared in very pure crystalline condition. A change in the value for the amide of xylonic acid would not affect the value of the rotation of the α-carbon atom but would alter those of the β- and γ-carbons. The alternation in sign of the successive carbon atoms is again apparent, and likewise the decrease in the rotation as the carbon atom is further removed from the amide end. The numerical value for the α-carbon, 44.5(10)^2, is quite near those that have been found for this carbon in the hexonic and heptonic acids, showing that the principle of optical superposition holds fairly closely for these amides.

Lastly, mention is made of the diamides of 3 of the dibasic acids of the sugar group, *d*-mannosaccharic and *d*-saccharic acids and tartaric acid.

TABLE IV.—CONFIGURATIONS AND ROTATIONS OF THREE DIAMIDES.

Diamide	Fischer's configuration	Specific rotation.	Molecular rotation
d-Saccharic diamide.......	 $NH_2\overset{O}{C}.\underset{OH}{\overset{H}{C}}.\underset{OH}{\overset{H}{C}}.\underset{H}{\overset{OH}{C}}.\underset{OH}{\overset{H}{C}}.\overset{O}{C}NH_2$	+13.3	+27.7(10)^2
d-Mannosaccharic diamide..	 $NH_2\overset{O}{C}.\underset{OH}{\overset{H}{C}}.\underset{OH}{\overset{H}{C}}.\underset{H}{\overset{OH}{C}}.\underset{H}{\overset{OH}{C}}.\overset{O}{C}NH_2$	—24.4	—50.8(10)^2
Tartaric diamide..........	 $NH_2\overset{O}{C}.\underset{H}{\overset{OH}{C}}.\underset{OH}{\overset{H}{C}}.\overset{O}{C}NH_2$	+106.5[1]	+157.6(10)^2

If the active carbon atoms in these structures be named in the manner that has been followed for the monoamides one must name from each end towards the center and in giving a sign to the rotations of the carbons of the left half must consider the structure to be turned through 180° in the plane of the paper, so as to put the left hand amide group around to the right end. Thus the 4 asymmetric carbons in *d*-saccharic diamide would be given the following signs and designations:

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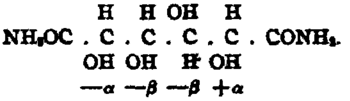
[1] Measurement by Frankland and Slator, *J. Chem. Soc.*, 83, 1354 (1903).



$$\begin{array}{ccccccccccc} & & \text{H} & & \text{H} & & \text{OH} & & \text{H} & & \\ \text{NH}_2\text{OC} & . & \text{C} & . & \text{C} & . & \text{C} & . & \text{C} & . & \text{CONH}_2 \\ & & \text{OH} & & \text{OH} & & \text{H} & & \text{OH} & & \\ & & -\alpha & & -\beta & & -\beta & & +\alpha & & \end{array}$$

Two equations may now be set up for the molecular rotations of the diamides of *d*-saccharic and *d*-mannosaccharic acids, respectively.

d-Saccharic diamide $-\alpha - \beta - \beta + \alpha = +27.7(10)^2$.

d-Mannosaccharic diamide $-\alpha - \beta - \beta - \alpha = -50.8(10)^2$.

Solving these two equations for the two unknown quantities gives $\alpha = +39.25(10)^2$ and $\beta = -13.85(10)^2$.

In the case of tartramide there are two α-carbons, both to be considered positive, and no β-carbons, hence $2\alpha = +157.6$ and $\alpha = +78.8(10)^2$.

The values for the carbons of the hexaric diamides are near those for the hexonic monoamides and are of the same sign. In the case of the tartaric diamide the sign is the same for the α-carbon but its numerical value is much larger, possibly because the two α-carbons, of strong rotation are not separated in this structure by any intervening carbon atoms.

It would be desirable to extend this study to the amides of other optically active dibasic acids. The present data are sufficient to allow the calculation, of the rotatory powers of the diamides of all the hexaric acids.

TABLE V.—MOLECULAR ROTATIONS OF THE ACTIVE CARBON ATOMS OF AMIDES FROM THE SUGAR GROUP.

Carbon	4-Carbon series, diamide	Pentonic amides	Hexonic amides.	Heptonic amides	Hexaric diamides.
α[1]..... . .	$+78.8(10)^2$	$+44.5(10)^2$	$+47.25(10)^2$	$-45.85(10)^2$	$+39.25(10)^2$
β..........	.....	$-23.15(10)^2$	$-14.65(10)^2$	$-19.6\ (10)^2$	$-13.85(10)^2$
γ..........	.....	$+\ 5.75(10)^2$	$+\ 0.95(10)^2$	?	......
δ..........	.....	......	$-\ 2.05(10)^2$	$-\ 4.2\ (10)^2$	......
ϵ..........	.....	......	......	?	......

In Table V are recorded the values that have been adduced for the molecular rotations of the different carbon atoms in these various amides. The values for the β- and γ-carbons of the pentonic amides depend upon Weerman's value for xylonic amide. We suspect that his value is slightly too high. If the rotation of the γ-carbon many be neglected in the pentonic amides, as seems probable from its low values in the hexonic series, the value of the rotation of the β-carbon can be calculated without using Weerman's determination. It is found to be $-17.4(10)^2$, which is near the average of the values that have been found in the hexonic and heptanic series. Using this value and neglecting that of the γ-carbon, gives for xylonic amide the rotation of arabonic amide, +37.5°, in place of Weerman's measurement, +44.5°.

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[1] With the formula of the compound written vertically and the amide group placed at the top, if the OH group of the particular carbon atom is on the right of the structure the sign of rotation of the carbon is that given in the table.

Experimental.

d-Galactonic Amide was prepared by passing dry ammonia gas into an absolute alcoholic solution of pure galactonic lactone, as described by Weerman. It was recrystallized 4 times from water and dried at 70° for 15 hours, and in another case at 100° for 7 hours. The two products showed the same specific rotation. 2.500 g. of substance dissolved to 50 cc. in water rotated at 20° in a 4 dcm. tube in sodium light 6.04 circular degrees to the right, hence $[\alpha]_D^{20}$ = +30.2°. Its melting point was 172–172.5°.

d-Gluconic amide was prepared similarly, crystallized 3 times from 90% alcohol and dried at 70° for 25 hours. Its m. p. was 143–4°. 2.500 g. of substance, made up to 50 cc. in water, rotated 6.24° to the right in a 4 dcm tube; hence $[\alpha]_D^{20}$ = +31.2. A second measurement gave the same value.

d-Gulonic amide was prepared by adding alcohol to a solution of 10 g. of gulonic lactone in strong ammonia water. The crystals were recrystallized from alcoholic solution twice and dried at 70° for 20 hours. M. p. 122–3°; yield 10 g. 2.500 g. of substance, dissolved to 50 cc. in water rotated 3.03° to the right in a 4 dcm. tube; hence $[\alpha]_D^{20}$ = +15.2

d-Mannonic amide was prepared by passing dry ammonia into an alcoholic solution of mannonic lactone. It was recrystallized from aqueous alcohol twice and dried at 70° for 20 hours. M. p. 172–3°. 0.4710 g of substance in 50 cc. aqueous solution rotated 0.65° to the left in a 4 dcm tube; hence $[\alpha]_D^{20}$ = −17.2. A second determination gave −17.4°, and the average is −17.3°.

α-d-Glucoheptonic amide was prepared by passing dry ammonia into an alcoholic solution of the lactone, was recrystallized from alcohol twice and dried at 70° for 10 hours. M. p. 134.5°. 0.3668 g. of substance in 25 cc aqueous solution rotated 0.31° to the right in a 2 dcm tube; hence $[\alpha]_D^{20}$ = +10.6

β-d-Glucoheptonic amide was prepared by passing dry ammonia into an alcoholic solution of the pure lactone. The lactone showed a specific rotation of −66.0° and m. p. 152–3°, in agreement with the values (−67.7° and m. p. 151–2°) that have been found by Fischer.[1] The amide was recrystallized twice from aqueous alcohol and dried at 70° for 24 hours. M. p. 158°. From 17.5 g. lactone 7.5 g. pure amide was obtained. 2.500 g. of substance in 50 cc. aqueous solution rotated 6.00° to the left in a 4 dcm. tube; hence $[\alpha]_D^{20}$ = −30.0°. A second measurement showed −30.3, and the average −30.2 is taken.

α-d-Galaheptonic amide was prepared according to Fischer's[2] directions, recrystallized twice from alcohol and dried at 70° for several hours. M. p. 206°. 0.2159 g. of substance in 50 cc. aqueous solution rotated 0.25° to the right in a 4 dcm. tube; hence $[\alpha]_D^{20}$ = +14.5. A second measurement showed +14.1 and the mean is taken, +14.3°.

l-Arabonic amide was prepared from ammonia and the lactone and was recrystallized twice from 90% alcohol, and dried at 70° for 18 hours. M. p. 135–6°. 2.500 g. of substance in 50 cc. aqueous solution rotated 7.43° to the right in a 4 dcm. tube; hence $[\alpha]_D^{20}$ = +37.2. A second estimation gave +37.9 and the mean is taken, +37.5°.

[1] *Ann.*, 270, 64 (1892).

[2] *Ibid.*, 288, 139 (1895).

***l*-Ribonic amide** was prepared from ammonia and the lactone. The latter was prepared from arabonic acid by rearrangement on heating with pyridine, according to Fischer[1] and Piloty's directions. The amide was recrystallized twice from 90% alcohol and dried at 70° for several hours. M. p. 137–8°. 0.8450 g. of substance in 25 cc. aqueous solution rotated 1.11° to the left in a 2 dcm. tube; hence $[\alpha]_D^{20} = -16.4$. Weerman found m. p. 136–7° and $[\alpha]_D^{20} = -15.7$.

***d*-Mannosaccharic diamide** was prepared according to Fischer's[2] directions by dissolving pure *d*-mannosaccharic dilactone in strong ammonia water, filtering off the crystalline precipitate and washing it with alcohol and ether. It was recrystallized once from water and dried at 70° for 14 hours. M. p. 188–189.5° with decomposition. 0.1765 g. of substance in 50 cc. aqueous solution rotated 0.36° to the left in a 4 dcm. tube; hence $[\alpha]_D^{20} = -24.4$. A second estimation gave —24.5. Fischer found m. p. 189°.

d-Saccharic diamide was prepared by the interaction of diethyl *d*-saccharic ester and ammonia, following Heintz's[3] directions It was recrystallized twice from alcohol and dried at 100° for 5 hours. M. p 172–3°. 0.8572 g. of substance in 50 cc. aqueous solution rotated 0.91° to the right in a 4 dcm. tube, hence $[\alpha]_D^{20} = +13.3°$.

WASHINGTON, D C

[CONTRIBUTION FROM THE SHEFFIELD CHEMICAL LABORATORY OF YALE UNIVERSITY.]

RESEARCHES ON PROTEINS. VI. THE DESTRUCTIVE DISTILLATION OF FIBROIN.

[PRELIMINARY PAPER.]

BY TREAT B JOHNSON AND PETER G. DASCHAVSKY.

Received June 7, 1919

This preliminary report of an investigation, now in progress in this laboratory, is made in order to announce our intention of incorporating in our Researches on Proteins the study of the products of decomposition when silk fibroin is subjected to destructive distillation *in vacuo*. The research will not be completed for several months, but in the light of the recent work of Pictet and Cramer[4] on the destructive distillation of ovalbumin it seems necessary to make known at this time our activity in this same field of research.

Very little is known regarding the nature of the products of decomposition which are formed by the distillation of protein material. While much attention has been paid to the chemistry of coal distillation and also destructive distillation of wood and cellulose material, so far as the writers are aware, no important literature has been contributed dealing with the dry distillation of proteins outside of that bearing on the production of Dippel's oil by distillation of bones. The only publications available to us which contribute any data on this subject are those of

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[1] *Ber.*, 24, 4214 (1891).

[2] *Ibid.*, 24, 539 (1891).

[3] *Pogg. Ann.*, 105, 211 (1858).

[4] *Helv. Chim. Acta*, 2, 188–195 (1919); *C. A.*, 10, 1076 (1919).

Limpricht[1] and Williams[2] describing the distillation of horn and wool, respectively, in the presence of potash. In both cases the only organic combinations that were definitely identified among the products of distillation were carbon dioxide and several aliphatic bases, namely: ethyl, butyl and amyl amines. These combinations undoubtedly resulted as normal products of decomposition of the corresponding α-amino acids present in the protein molecule.

$$R.CH(NH_2)COOH \longrightarrow CO_2 + R.CH_2NH_2.$$

Later in 1885 Mills[3] subjected wool to dry distillation at ordinary pressure and identified as products of decomposition, hydrogen sulfide, water and ammonium carbonate.

Silk fibroin was selected for our investigation for three reasons. In the first place the protein is available in large quantities and can be obtained in a very pure condition. Secondly, it is one of the protein combinations which is free from sulfur, and thirdly, it is characterized by its amino acid composition. 60% of this protein molecule is composed of three amino acids, namely, glycocoll, alanine and tyrosine; these three acids constituting about 33%, 16% and 10%, respectively, of the fibroin molecule. Whether a careful study of the products formed by destructive distillation of proteins in general will contribute data throwing new light on the molecular construction of these substances remains to be determined, but it is true that fibroin is an excellent protein for experimentation on account of its unique composition.

Our method of experimentation has been to distil fibroin from an iron retort or pipe so constructed that the latter can conveniently be heated at a high temperature on an ordinary combustion furnace. Ordinary iron pipe of 5″ diameter has proven very practical for this operation. Having charged the retort with a known quantity of silk, it is then connected by the necessary cooling and absorption apparatus with a Cenco vacuum pump, which is sufficiently efficient to evacuate the system employed in our work. We first operated with a unit of 200 g. of fibroin (silk noils), but we finally increased this to 1600 g., which we found to be a very convenient and practical unit for laboratory operations. Working under these conditions, we have successfully distilled several kg. of silk fibroin, and the products of distillation are now being studied in order to determine the relative quantities formed, the compositions and the characteristic properties.

When distilled *in vacuo* (25–27 mm.) silk fibroin affords about 43% of its weight in the form of a red oil distillate, 41% in the form of silk carbon or coke and 16% in the form of volatile and gaseous products which

[1] *Ann. Pharm.*, **101**, 297 (1857).

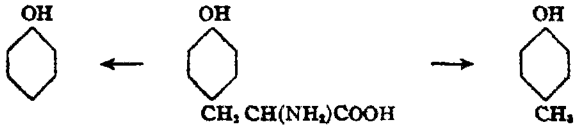
[2] *Ibid.*, **109**, 127 (1858).

[3] *J. Soc. Chem. Ind.*, **4**, 325 (1885).

are absorbed by sodium hydroxide solution and sulfuric acid. The quantity of red oil distillate obtained varies from 660 to 790 g. per 1600 g. of fibroin, depending apparently to a large degree upon the pressure maintained during distillation of the protein. Thus far the only fraction which has received careful attention by us is the red oil distillate which is now under investigation. This is strongly ammoniacal and contains a large proportion of water besides organic substances of phenolic character.

We desire to report now on the isolation and identification of phenol among the components of this red oil distillate. This was separated in the following manner· An aliquot part of the oil distillate was subjected to steam distillation to remove the phenol and the latter then extracted from the steam distillate with ether and finally distilled under diminished pressure. We obtained an oil boiling from 48–58° under a pressure of 3 mm. This product was redistilled at ordinary pressure and finally washed with a 10% solution of sodium hydroxide to separate it from non-phenolic combinations. An oil having a pyridine odor was obtained here insoluble in the alkali On acidifying the alkaline solution, after separating from insoluble oil, the phenol separated at once and was extracted with ether and again purified by distillation. It distilled as a colorless oil boiling at 182.5–185° at ordinary pressure. This product possessed all of the characteristic properties of carbolic acid, namely, odor and solubility in alkali and water, and it also gave the characteristic color test with ferric chloride. It reacted with bromine and nitric acid to give the characteristic insoluble tribromophenol, $C_6H_2(OH)Br_3$ (m. p. 89°), and picric acid, $C_6H_2(OH)(NO_2)_3$ (m. p. 122°), respectively.

Whether cresol is one of the products of distillation of fibroin has not yet been established Both of these two phenols might result from the breaking down of tyrosine in the protein molecule. Quantitative experiments will be made in order to determine what portion of the tyrosine in the protein molecule breaks down by distillation in this manner. It will also be of interest in this connection to subject polypeptide combinations of tyrosine to dry distillation *in vacuo.*



NEW HAVEN, CONN

NEW BOOK.

Helvetica Chimica Acta. Vol. I, No. 1. Editors: E. BOSSHARD, FR. FICHTER, PH. A. GUYE, A. PICTET, H. RUPE, A. WERNER. Published by the Swiss Chemical Society. Issued by George & Company, Basel and Geneva.

This new chemical periodical represents the response of Swiss chemists to the present world-wide wave of nationalism. Ph. Guye, President of the Swiss Chemical Society, in the Foreword of the first volume, points out the necessity of some such Journal for his Society, now (1918) seventeen years old. He also gives the interesting information that during 1914, 380 articles on chemical subjects emanated from Swiss laboratories. Some 22 Swiss chemical manufacturing firms have established a guarantee fund to insure the financial success of this venture. The articles in this journal are to be in the three official languages of the country, namely, French, German and Italian.

The first number contains articles by several of Switzerland's most distinguished chemists, and establishes a high standard of excellence, as can be seen in the following table of contents:

A. WERNER: A New Variety of Isomerism in Compounds of Cobalt and Compounds Containing Asymmetric Cobalt and Carbon

PH. A. GUYE AND FRITZ SCHNEIDER: Reduction of the Oxides of Nitrogen to Ammonia; the Stability of Nitrogen Dioxide

TH. GASSAMAN· The Occurrence of Hydrogen Selenide in Rain and Snow

A. WERNER AND P. KARRER: Nitroso-Pentammine Cobaltic Salts

A. WERNER AND SOPH MATISSEN· On the Constitution of Internally Complex Metallic Salts.

ALFRED BERTHOUD: Determination of the Surface Tension and Critical Density of Ammonia.

AMÉ PICTET AND JEAN SARASIN: On the Distillation of Cellulose and Amidon under Reduced Pressure.

The printing, paper and general appearance of this periodical are excellent, and cannot but provoke our admiration and indeed envy.

We congratulate the Swiss Chemical Society and the Board of Editors on this first number of "Helvetica Chimica Acta" and welcome this new addition to the chemical literature of the world. May it serve to give wider attention and recognition to the work of Swiss chemists, and thus help to accelerate the forward progress of our Science.

ARTHUR B. LAMB.

VOL. XLI. AUGUST, 1919. No. 8.

THE JOURNAL

OF THE

American Chemical Society

with which has been incorporated the

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(Founded by Ira Remsen)

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ARIZONA.]

THE SINGLE DEFLECTION METHOD OF WEIGHING.

BY PAUL H M.-P. BRINTON

Received February 19 1918

Of the routine manipulations required in chemical analysis few are more important, and at the same time more tedious, than the operation of weighing, and any shortening of the time necessary for this would be a great help. Routine analysts usually find short cuts, but the research worker who carries though his analyses with a different end in view, and gives less thought to simplifying manipulative details, frequently wastes much time and patience in the use of the balance. The method described in this paper has been adopted after exhaustive tests as to its reliability and rapidity, and it seems only fair to offer to others the advantage of the great saving of time which this system effects, without the sacrifice of essential accuracy. The method was brought to the writer's attention a number of years ago by Dr. F. N. Guild, of the University of Arizona, who had used it for many years, but could not give the source from which it originally came. So far as can be learned, the procedure has never been described in book or journal, with the exception of a short paper by Turner.[1] It is believed that the method is almost unknown, and is used in very few laboratories. Those who have heard the method mentioned probably regard it with the same scepticism as did the writer, who refused to even try it for 10 years, so unorthodox did the system appear; and so little faith did he have that any degree of accuracy was obtainable by so simple a procedure.

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[1] *Chemist-Analyst*, January, 1916.

The method is carried out as follows: The balance is given a permanent overload on the left arm by screwing the adjusting nut on one end of the beam until when the beam and pans are released the pointer will swing out from 3 to 7 scale divisions to the right. The pan arrests must be so adjusted that there is no lateral vibration of the pans when released. Before determining the zero point the stability of the pans is assured by moving the pan-arrest button in and out a few times. The beam is then freed, and the pans are next released by a gentle, steady motion. The pointer will swing out to the right, and the turning point of this single excursion is taken as the zero point. To obtain the weight of any object it is only necessary to add weights until the pointer is caused to swing out to the same point on the ivory scale. The convenience and rapidity of the method were immediately apparent, but grave doubts were entertained as to its practicability and reliability until confidence was established by critical investigation.

Constancy of Deflection.

A Becker aluminum balance was used, and 4 sets of weighings were made, each consisting of 9 observations. The deflection readings are shown in Table I. The 4 sets were made in determining the sensibility of the balance with empty pans, and with 50 g. loads, so concordance between A and D, and between B and C, is not to be looked for. The arithmetical mean of each set has been calculated, and also the value of d/s, in which d represents the maximum deviation from the arithmetical mean in each set, and s the sensibility of the balance in scale divisions per milligram.

TABLE I.

										Mean	d/s
A.........	3.7	3.75	3.8	3.75	3.8	3.8	3.75	3.8	3.75	3.77	0.015
B.........	8.8	8.8	8.8	8.85	8.75	8.8	8.75	8.85	8.8	8.80	0.010
C.........	8.65	8.7	8.6	8.6	8.6	8.65	8.65	8.65	8.6	8.63	0.015
D.........	3.6	3.6	3.6	3.6	3.6	3.6	3.6	3.6	3.55	3.60	0.010

It will be seen that with this balance the constancy of deflection fulfils the strictest demands of accuracy, for the values of d/s indicate that the greatest error of observation in this step will probably not exceed 0.015 mg. The weighings were made by an experienced manipulator, with a splendid balance, ideally situated, and with a reading lens for observation of deflections. To give the method a more thorough trial, experiments were made with a section of 10 average students who had never handled an analytical balance (although 3 had had a course in assaying). These men were assigned to balances which cost from $35 to $75 each, selected at random in the regular student balance room. Each student made 4 sets of weighings, with 5 to 7 observations in each set. The sensibilities of the balances registered from 2.6 to 4.9 scale divisions per milligram. In Table II are recorded the values of *d/s*, in which *d* was taken as the greatest deviation from the mean in any set for each student. The number of readings by each observer was from 20 to 28.

TABLE II.

Student	1	2	3	4	5	6	7	8	9	10
d/s	0.03	0.10	0.03	0.06	0.06	0.04	0.08	0.06	0.03	0.03

From this it is seen that in the work of entirely inexperienced students, with ordinary balances, any error introduced through inconstancy of deflection will probably not exceed 0.1 mg. These students had no idea that their results were to be tabulated for publication, and it is certain that further practice in weighing would increase the accuracy of their observations.

In order to test the effect of one's prejudice in favor of making all subsequent readings in any one set agree with the estimate made in the first observation, the same 10 students were asked to read the deflection on one high grade balance. Only one student was allowed in the room at at a time, so no mental prejudice was operative. The observations extended over a period of two hours, and the deflection was determined at intervals by the writer, whose readings are shown under the asterisks in Table III. Each student made 5 to 7 observations, and in the case of only one operator did a deviation from the mean as great as 0.1 scale division occur. The sensibility of the balance was 5.0.

TABLE III.

Student	*	1	2	3	4	*	5	6	7	8	9	10	*
Deflection	3.7	3.7	3.8	3.7	3.8	3.8	3.8	3.8	3.8	3.8	3.9	3.8	3.85

From the writer's observations it seems probable that the zero point shifted a tenth of a division or so during the period, and taking this into account one must be struck by the concordance of the readings of 11 experimenters, 10 of whom were inexperienced.

For those trying the method on a very sensitive balance it is suggested that attention be paid to the effect of the currents of air, or the lengthening of the beam, caused by the heat of the hand near one pan, for it will be found that the first swing does not always accord with those which follow. This method is so rapid that irregularities are easily detected which would frequently escape observation by ordinary manipulation.

The balance case had been closed a long time, and these deflection readings were taken:

3.9 3.9 3.9 3.9 3.9 3.9

The hand was then held 15 seconds near the left pan, and as soon as the door had been closed, the following series of observations was begun:

4.0 3.95 3.9 3.9 3.9

The experiment was repeated, holding the hand near the right pan for 15 seconds, with the following results:

3.6 3.9 3.95 3.9 3.95

It is seen that with a sensitive balance a few moments must be allowed for abatement of jar and air currents, but equilibrium is soon re-established. This is not to be construed as a criticism peculiar to this particular method, for it will be understood that the same precaution is necessary with any system of weighing.

Behavior with Various Loads.

Two faults frequently found in balances, especially in those of cheaper grade, are varying sensibility under increasing load, and inequality in the lengths of the two lever arms. It is evident that both these conditions would influence the accuracy of absolute weighings by the single deflection method, but in nearly every instance in analytical work the weighing consists in comparing the weight of an empty vessel (watch glass, crucible, or dish) with that of the same vessel containing at most a few grams of sample or ignited precipitate. Manifestly, then, the error introduced by varying sensibilities, or by inequality of arms, would be negligible in nearly all cases of analytical practice. The method has been successfully used by students in calibrating weights by the method of Richards,[1] and a few hours only are required by even a beginner for the calibration of a full set of weights.

Precautions and Limitations.

The single deflection method of weighing cannot be used with those types of balances in which the beam and pan-arrests are all released by one operation, as by the turning of one milled head or lever; and it has occasionally been found that a balance of the correct general type has failed to give concordant readings in successive weighings. In nearly every instance it has been found that these balances failed to yield concordant weighings by any other method.

The pan-arrests must be clean and adjusted to the proper height. A little alcohol will remove any grease which might tend to cause sticking of the pan-arrest to the bottom of the pan.

A little experience with a particular balance will soon show one just how far the method can be trusted with that instrument. With the balance habitually used by the writer, which has an unvarying sensibility with loads up to 50 g., the method is regarded as suitable to work of the very highest accuracy. It is realized that the error of a single observation should be greater than that of the mean of 3 or 5 observations, but it may be pointed out that it is much easier to read with the highest accuracy when the swing is to one side only, and does not cross a center point.

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[1] This Journal, 22, 144 (1900).

Furthermore, the chance for lapse of mental concentration and attention is greatly diminished in the single deflection method. In work of great importance the weighing can be checked by a second weighing in less time than is needed for one weighing by the conventional methods.

It is certainly not advisable to teach this method to students as their sole equipment for weighing operations, for a number of good balances on the market are of the "single release" type; but with proper emphasis on the limitations of the process the single deflection method can be given to students with great benefit. An analyst who will weigh out a 3-g. sample of steel, for determination of phosphorus, with an accuracy greater than within one mg., has little greater chance of success in the world than he who will weigh out a 0.2-g. sample of copper foil, for standardizing, with an acuracy less than within 1 mg.

TUCSON, ARIZONA.

[CONTRIBUTION FROM THE KENT CHEMICAL LABORATORY OF THE UNIVERSITY OF CHICAGO.]

INTERMEDIATE AND COMPLEX IONS. V. THE SOLUBILITY PRODUCT AND ACTIVITY OF THE IONS IN BI-BIVALENT SALTS.[1]

BY WILLIAM D. HARKINS AND H. M. PAINE.

Received October 3, 1918[2]

The first evidence which indicates that *all salts* which give, on complete ionization, 3 or more ions, ionize in steps in such a way as to give intermediate ions, was presented by Harkins[3] in 1911. The earlier idea was that intermediate ions are present in aqueous solution of some of the salts of higher types, but not in all cases. Thus Abegg and Spencer,[4] in 1905, considered that thallous oxalate gives rise to an intermediate ion, but potassium oxalate does not, while in 1911 Jellinek[5] concluded that intermediate ions are present in solutions of sodium sulfate, but not when potassium sulfate is the solute. Such salts are mercuric chloride, cadmium chloride, and lead chloride were commonly believed to give intermediate ions, but the more ordinary salts were in general supposed to ionize in one step or else to give only a negligible fraction of intermediate ions. Perhaps the strongest evidence in favor of ionization in one step was found in the fact that in solutions of uni-bivalent salts the transference number is independent of the concentration. The work of Harkins indicates, however, that the percentage of intermediate ion is not negligible, but for salts of the type of potassium sulfate is 18% for 0.01 *N* solutions, 35% at 0.1 *N*, and rises to 46% in a normal solution, these being the percentages for the KSO_4^- ion.

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[1] This series of papers was begun by the senior author in the Research Laboratory of Physical Chemistry of the Massachusetts Inst tute of Technology and has been continued in the laboratory of the University of Chicago with the consent of Professor A. A. Noyes.

[2] Revised manuscript received April 21, 1919. The paper was completed, except for minor changes, in June, 1914.

[3] THIS JOURNAL, 33, 1836–72(1911); Harkins and Pearce, *Ibid.*, 37, 2679 (1916).

[4] *Z. anorg. Chem.*, 46, 406 (1905).

[5] *Ibid.*, 76, 309 (1911).

In a study of the solubility of uni-bivalent salts it was found that whereas the addition of a salt with a common univalent ion decreases the solubility of the uni-bivalent salt very greatly, just as would be expected, the addition of a salt with a common bivalent ion has an entirely different effect from what had previously been supposed. In other words, the solubility curve in the latter case, at least where the saturating salt has a solubility of 0.05 *N* or more, has another form than that which would be predicted from the solubility product principle upon the basis of the usual assumptions. Instead of falling rapidly as the concentration of the added salt increases, the solubility of the saturating salt decreases[1] at first slightly but then increases.

When salts of the bi-bivalent type are used as saturating salts it is impossible to add a salt with a common univalent ion; but when salts with *bivalent* common ions are added to solutions of calcium sulfate (see Fig. 1), the solubility curves have somewhat the same form as when the saturating salt is of the uni-bivalent type. The explanation given by Harkins for the peculiar solubility curve of the uni-bivalent salts, was that it is due to the presence in such solutions of a considerable percentage of intermediate ions such as KSO_4^-, $BaCl^+$, etc.

It was found that the presence of intermediate ions in solution could also be easily recognized from the slope of the curve representing the solubility of the un-ionized part of the saturating salt when the concentration of the un-ionized part is calculated on the basis of the usual assumptions, which are as follows: (1) That the isohydric principle is valid, (2) that the usual method of calculating percentages ionization is correct, and (3) that no intermediate ions are present in the solution. Now, it happens that the deductions obtained by this method of detecting intermediate ions hold in all probability even if (1), the isohydric principle is not valid, and (2) if the usual method of calculating the percentage ionization is incorrect. This is true because no use is made of the absolute values of the solubility of the un-ionized part of the salt as calculated, and the only essential feature of the method is a proper comparison of the slopes of the calculated solubility curves for the non-ionized parts of uni-univalent and uni-bivalent salts. Thus, when calculated in the usual way, such curves for the *uni-univalent* salts slope rapidly downward as the total ion concentration (or the concentration of the added salt) increases. Now, if similar curves are constructed for *uni-bivalent* salts, it might be expected that they would have a somewhat similar form, and this is exactly what is found when the added salts used are such as would have little effect upon the calculated solubility of the un-ionized part when intermediate ions are present. The only salts of this kind are those with *no common ion.* In this case the curves for uni-univalent and uni-bivalent salts lie almost exactly parallel (compare with Fig. 3). However, when the added salt contains a common bivalent ion, the curves, when calculated on the basis of the third assumption, *i. e.*, that no intermediate ions are present, should not show the same slope if intermediate ions are present in considerable quantity. From the change in the slope of the curve it would be possible to form some idea of the amount of the intermediate ion present, although a quantitative estimate can be made much more accurately by the use of other methods. Now, if intermediate ions are present in the saturating salt, the calculated solubility of the un-ionized part should decrease much more rapidly when the added salt contains a common univalent ion, and, on the other hand, when a salt containing a common bivalent ion is added, this solubility should either decrease *less* rapidly or if the relative number of intermediate ions is large, the calculated solubility curve should rise instead of falling, and this latter has been found to be the case for uni-bivalent salts. It will be seen that this method of showing the presence of intermediate ions, and also something of their relative amount, depends upon the deviation of the calculated solubility curves from the normal slope, since at least the greater part of the deviation is caused by the false assumption that intermediate ions are absent.

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[1] In the case of highly soluble salts of this type this initial decrease is absent, and the curves have the form which would be expected if the added salt had no ion in common with the saturating salt.

When it is realized that more than half of the salts commonly used are higher type salts, it will be seen that it is important to extend this investigation to a study of types still higher than the uni-bivalent type already studied.[1] The next most important type of salts is the bi-bivalent; and in this type of salts there is a reversion from the tri-ionic salts previously investigated to di-ionic salts, which, with respect to the number of ions formed by a simple ionization, would seem to belong to the same type as the di-ionic uni-univalent salts. Since, by their simple ionization the bi-bivalent salts would give the same number of ions per molecule it might be expected that the curve for the solubility of the un-ionized part should be of the same general form as for the uni-univalent salts, provided that the ionization of the bi-bivalent salts is entirely a simple one.

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[1] Harkins and Pearce, THIS JOURNAL, 37, 2679 (1916) have shown that uni-trivalent salts give a large number of intermediate ions in solution.

In view of these interesting ionization relations of trionic and still higher type salts, a study of sparingly soluble bivalent salts was undertaken with calcium sulfate as a type salt of this group. Its solubility and conductance were determined in pure water and also in solutions of various concentrations of copper sulfate, magnesium sulfate, and potassium nitrate. Density determinations were made on all mixtures and all weighings were corrected to vacuum. In the calculations the atomic weights for 1910 were used.

Preparation of Salts and Solutions.

The water used for this investigation had in no case a greater specific conductance than 0.7×10^{-6} and the average value in the bottles in which it was stored was 0.6×10^{-6}.

Calcium Sulfate.—This salt was made by the addition of a very dilute potassium sulfate solution to to very dilute calcium chloride solution. Kahlbaum's "Zur Analyse" salts were used and the work carried out in special vessels of resistance glass. The calcium sulfate was washed thoroughly and rotated with several successive portions until the conductivity became constant. This salt was preserved in glass-stoppered resistance glass bottles.

Gypsum.—For comparison some very clear plates of gypsum were obtained from Dr. A. D. Brokaw of the Geology Department.

Magnesium Sulfate—Kahlbaum's "Zur Analyse" salt was twice recrystallized from conductivity water and a stock solution made up and analyzed by evaporation in platinum and weighing as magnesium sulfate.

Copper Sulfate.—Kahlbaum's "Zur Analyse" salt was twice recrystallized from conductivity water.

Potassium Nitrate.—Baker's potassium nitrate was recrystallized twice from conductivity water.

Methods of Analysis.

Calcium.—Calcium was determined by careful precipitation with ammonium oxalate from hot solution; after standing 4–6 hours, the calcium oxalate was filtered, washed with water containing a little ammonium oxalate, ignited in tared platinum crucibles and weighed as calcium oxide Where copper was present it was removed from a very dilute solution by precipitation with hydrogen sulfide. The separation of magnesium from calcium presented difficulties because of the well-known fact that the quantitative separation of small amounts of calcium from much larger amounts of magnesium is unsatisfactory. The method proposed by Cameron and Bell[1] leaves much to be desired from th standpoint of accuracy A plate of pure gypsum rotated in 25 cc. of conductivity water showed a loss equivalent to solubility of 2.067 g. per 1000 g. solution. The solution from this gave 2.083 g. $CaSO_4$ per 1000 g. of solution by the oxalate method, while the specific conductance was 0.0022115 ohms, almost the same as tha for the prepared salt (0.0022148). This method was used therefore only in solutions of comparatively high concentration of magnesium sulfate. For the more dilute solutions the method proposed by Richards, McCaffery and Bisbee[2] was used.

Experimental Methods.

An excess of the calcium sulfate was rotated with water or solution of a salt in a 500 cc. glass stoppered resistance glass bottle which had been "steamed out" and thoroughly seasoned. The temperature was measured by a thermometer which had been compared with a certified Baudin thermometer. For each determination saturation was approached both from under-saturation and supersaturation. The solutions were filtered in the thermostat and the first 50 cc. rejected, in order to prevent errors due to adsorption. In the experiments with copper sulfate the concentration of copper was determined for each bottle separately. In the other series solutions were carefully made up in calibrated flasks from a weighed amount of standard solution. The calcium sulfate was finally carefully washed on a platinum cone with a large amount of the solution, and quickly transferred to the bottle, which was then filled up with solution and rotated as usual.

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[1] *J. Phys. Chem.*, 10, 212 (1906).

[2] *Proc. Am. Acad.*, 36, 375 (1901).

The conductivity measurements were made in the usual way with a roller bridge carefully standardized. The apparatus was similar to that used by Washburn.[1] Great care was taken throughout the work to exclude carbon dioxide from the solutions. The bottles were all filled with carbon dioxide-free air and all solutions and water carefully protected from contact with the air by soda lime trains.

Experimental Data.

The results of the solubility determinations of calcium sulfate in solutions of copper sulfate are given below in Table I, in Potassium nitrate in Table II*a*, in magnesium sulfate in Table II*b*, and those for gypsum in magnesium sulfate in Table II*c*.

The solubility of calcium sulfate in solutions of copper sulfate, magnesium sulfate, and potassium nitrate, together with the conductances of all of the solutions of the pure salts and of the mixtures, were determined by us, because none of the previous work on calcium sulfate gave extensive enough conductivity data for our purpose. The solubility data are plotted as undotted lines in Fig. 1, while the dotted lines represent the work of Cameron with potassium and sodium sulfates as the added salts. Other data of a similar nature may be found in papers by Sullivan[2] and by Cameron[3] and his associates.

The curves in this figure, which represent the addition of the common bivalent ions, do not have the form to be expected when a common ion is added, in fact, as is shown most clearly in Fig. 1, at a very low concentration (0.15 *N*) the copper sulfate curve changes to the form to be expected when a salt with no common ion is added, while that for magnesium sulfate changes at about 0.35 *N*. The form of these curves is somewhat the same as that previously found when a salt with a common bivalent ion is added to a solution in which the saturating salt is unibivalent and has a solubility of 0.07 *N* or more. The principal difference is that the initial solubility drop is greater in the case of the bi-bivalent salts. This change in the form of the curves representing the common ion effect has

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[1] THIS JOURNAL, 35, 177 (1913).

[2] *Ibid.*, 27, 532 (1905).

[3] Cameron and Seidell, *J. Phys. Chem.*, 5, 643–55 (1901); Cameron, *Ibid.*, 5, 56 (1901); Seidell and Smith, *Ibid.*, 8, 493 (1904); Cameron and Bell, THIS JOURNAL, 28, 1220 (1906); Cameron and Bell, *J. Phys Chem.*, 10, 212 (1906); Cameron and Brezeale, *Ibid.*, 8, 337–40 (1904).

TABLE I.—SOLUBILITY OF CALCIUM SULFATE IN SOLUTIONS OF COPPER SULFATE.

Copper sulfate.				Calcium sulfate.					
Per liter of solution G.	Per 1000 g. solution G	Equivalents per liter of solution.	Per 1000 g water G	Per 1000 g solution G	Per liter solution G	Equivalent concentration per liter	Per 1000 g. water. G.	Specific conductance of mixture	d_4^{25} of mixture.
0.0	0.0	0.0	0.0	2.0854	2.0835	0.03064	2.0897	0.0022148	0.99911
1.9963	1.996	0.025010	2.002	1.8435	1.8458	0.027113	1.8511	0.0031580	1.0010
7.9758	7.922	0.099925	7.998	1.671	1.6823	0.024711	1.687	0.0061348	1.0069
16.082	15.842	0.20147	16.128	1.661	1.6860	0.024767	1.691	0.009680	1.0149
33.810	32.67	0.42358	33.838	1.7468	1.8037	0.026493	1.8093	0.016383	1.0324
155.01	134.65	1.9420	155.95	1.944	1.2333	0.032804	2.252	0.046627	1.1486

TABLE II.—SOLUBILITY OF CALCIUM SULFATE (*a*) IN SOLUTIONS OF POTASSIUM NITRATE.

G. salt added per liter of solution (KNO₃.)	d_4^{25} of added salt solution	Equivalent concentration per liter of solution (KNO₃)	G added salt per 1000 g water.	G added salt per 1000 g solution	G Ca SO₄ per 1000 g solution	G Ca SO₄ per liter of solution	Equivalent concentration per liter (CaSO₄)	G Ca SO₄ per 1000 g water	Specific conductance of mixture.	d_4^{25} of mixture
0	0	0	0	0	2.0854	2.0835	0.030604	2.0897	0.0022148	0.99911
2.786	0.99876	0.027554	2.797	2.7824	2.454	2.4571	0.036092	2.4669	0.0059355	1.0013
5.326	1.0004	0.052675	5.352	5.3106	2.7268	2.7347	0.040169	2.7489	0.0090808	1.0029
10.421	1.0036	0.10307	10.492	10.330	2.862	2.8870	0.42407	2.9002	0.014985	1.0088
(*b*) in Solutions of Magnesium Sulfate.										
(MgSO₄)		(MgSO₄)								
0.0	...	0.0	0.0	0.0	..	...	.	...	...	....
0.6027	0.9977	0.10013	0.6044	0.60294	1.9565	1.9557	0.028726	1.9615	0.0026642	0.99960
1.2168	0.9983	0.020216	1.2190	1.2167	1.848	1.8482	0.027148	1.8537	0.003139	1.0001
1.8331	0.999	0.030488	1.8403	1.8339	1.777	1.7781	0.026119	1.7834	0.0036181	1.00067
(*c*) Solubility of Selenite Plates in Solutions of Magnesium Sulfate.										
0	...	0	0	....	..	2.064	0.030317	2.0703	0.0022115	0.99905
0	...	0	0	....	..	2.055	0.030185	3.0613	0.0022115	0.99905
1.3376	...	0.022223	1.3413	....	..	1.7838	0.026201	1.7886	0.0034042	1.0004
3.3057	...	0.054921	3.3161	....	..	1.6417	0.024114	1.6469	0.0045499	1.0018
6.293	...	0.10455	6.3148	....	..	1.5538	0.022823	1.5592	0.0066165	1.0044
12.336	...	0.20495	12.385	....	..	1.4953	0.021964	1.5912	0.010415	1.0099

TABLE III —EQUIVALENT CONDUCTANCE OF MAGNESIUM SULFATE AT 18° AND AT 25°. (CONCENTRATIONS IN EQUIVALENTS PER LITER, CONDUCTANCE IN RECIPROCAL OHMS)

Concentration	$\Lambda_{18°}$	Λ/Λ_0	$\Lambda_{25°}$	Λ/Λ_0
0.00	135 0	100 00	114 4	100 00
0 00050635	123 3	91 33	101 7	91 52
0 0010047	117 4	86 96	100 1	87 50
0 0020094	110 8	82 08	94 67	82 75
0 005023	99 0	73 33	84 35	73 73
0 010047	88 85	65 82	76 15	66 56
0 020094	78 98	58 50	67 23	58 77
0 050235	66 05	48 93	56 54	49 37
0 10047	57 79	42 81	49 58	43 34
0 20094	49 82	36 90	43 12	37 69
0 50235	40 72	30 16	35 25	30 81
1 0067	33 37	24 72	28 81	25 18

TABLE IV —CONDUCTANCE OF CALCIUM SULFATE SOLUTIONS (a) AT 25°

Equivalents per liter × 10^3	Specific conductance × 10^4 1/ohm	Λ 1/ohm	Λ/Λ_0	d_4^{25}.
0 0		140 0	100 00	
0 099955	1 3657	136 63	97 59	
0 19955	2 650	132 88	94 91	
0 49795	6 343	127 38	90 98	
0 9959	12 104	121 57	86 84	
1 9975	22 612	13 20	80 86	0 99720
5 011	50 195	100 15	71 53	0 99748
10 081	90 17	89 45	63 89	0 99782
30 610	221 48	72 35	51 68	0 99911
36 408	252 0	69 21	49 44	(Hulett)

(b) AT 18°.

Equivalents per liter × 10^3	Specific conductance × 10^4 1/ohm	Λ 1/ohm	Λ/Λ_0	d_4^{18}.
0 0		119 00	100 00	..
0 10013	1 1644	116.28	97 80	.
0 19986	2 2670	113 43	95 32	..
0 49871	5 436	109 0	91 60	.
0 99755	10 407	103 82	87 24	.
2 007	19 446	97 19	81 67	
5 023	43 270	86 20	72 44	0 99895
10 096	77 96	77 21	64 88	0 99897

TABLE V —CONDUCTANCE OF COPPER SULFATE SOLUTIONS AT 25°.

Equivalent concentration	Specific conductance × 10^3 1/ohm	Λ 1/ohm	d_4^{25}
0 025156	1 7286	86 50	0 99950
0 050202	2 9688	59 13	1 0013
0 100081	5 0609	50 56	1 0053
0 201085	8 7545	43 53	1 0136
0 41993	15 535	36 99	1 0307
1 9335	46 082	23 83	1 14645

TABLE VI.

Ionization of Salts in Mixtures Containing (*a*) Copper Sulfate or (*b*) Magnesium Sulfate in which Calcium Sulfate is the Saturating Salt, Calculated on the Assumption that Complex or Intermediate Ions are not Present. (Concentrations in Equivalents per Liter.)

Total concn. ($CuSO_4$).	Solubility $CaSO_4$	Solubility un-ionized. $CaSO_4$	Concn. Ca^{++} ions	Σi or concn $SO_4^{=}$ ions	Solubility product $Ca^{++} \times SO_4^{=} \times 10^4$	Concn un-ionized ($CuSO_4$)	Concn ions (Cu^{++}).	Specific conductance of mixture × 10^3 Calc	Det
0.0	0.030604	0.014788	0.015816	0.015816	2.503	0.0	0.0	2.2142	2.2148
0.025010	0.027113	0.014353	0.012760	0.02376	3.032	0.01401	0.0110	3.2393	3.1580
0.09992	0.024711	0.015121	0.009590	0.04587	4.398	0.06365	0.03628	6.1352	6.1348
0.20147	0.024767	0.016197	0.008570	0.07285	6.243	0.13719	0.6428	9.6912	9.6798
0.42358	0.026493	0.018503	0.007990	0.12280	9.811	0.30878	0.1148	16.284	16.383
1.9420	0.032804	. . .	. .	. .	. .	. . .		. . .	46.627
($MgSO_4$.)						($MgSO_4$.)	Mg^{++}		
0.0	0.030604	0.014788	0.015816	0.015816	2.503	. .	0.0	2.214	2.11
0.010013	0.028726	0.014576	0.014150	0.01934	2.735		0.00519	2.681	2.664
0.020216	0.027148	0.014303	0.012845	0.02294	2.941	. .	0.01005	3.155	3.139
0.030488	0.026119	0.014210	0.01191	0.02655	3.162	0.01585	0.01464	3.645	3.618
0.054921	0.024114	0.014084	0.01003	0.03500	3.510	0.03002	0.0247	. . .	. . .
0.10455	0.022823	0.01392	0.00890	0.05190	4.630	0.06155	0.0430	. .	. . .
0.20495	0.021964	. .	. . . .	. . . .	. . .	. .	.	. . .	. . .

TABLE VII.

Ionization of Salts in Mixtures of Calcium Sulfate and Potassium Nitrate in which Calcium Sulfate is the Saturating Salt. (Concentrations in Equivalents Per Liter.)

Total concn. KNO_3	Total solubility. $CaSO_4$	Concn. $CaSO_4$ un-ionized.	Concn Ca^{++} ions	Concn $SO_4^{=}$ ions	Σi = total ion concentration	Solubility product Ca × $SO_4 \times 10^4$	Concn KNO_3 un-ionized	C_{K^+}.	$C_{NO_3^-}$.	$C_{(CaNO_3)_2}$.	$C_{K_2SO_4}$.	Specific conductance × 10^3. Calc.	Det.
0.0	0.030604	0.014790	0.01582	0.01582	0.01582	2.503	0.0	0.0	0.0	0.0	0.0	2.2142	2.2115
0.027554	0.036092	0.013553	0.01955	0.01955	0.04195	3.821	0.001779	0.0224	0.0224	0.00302	0.00348	6.008	5.936
0.052675	0.040169	0.01322	0.02192	0.02192	0.06400	4.805	0.00508	0.04207	0.04207	0.00503	0.00550	9.158	9.081
0.1236	0.04820	0.013126	0.02600	0.02600	0.1210	6.760	0.01872	0.0950	0.0950	0.009148	0.00970	. .	. .

been shown, in previous papers of this series, to be connected with the formation of complex ions, double salts, or intermediate ions

Another indication of the presence of intermediate or complex ions is that the solubility product as calculated from the solubility measurements increases more rapidly than when such ions are absent. This is because the calculations of the ionization count a part of the material present as intermediate, as being in the form of simple ions, and since the concentration of the intermediate ion increases rapidly with the concentration, this leads to an apparent rapid increase of the solubility product. It has been shown in a former paper that when account is taken of the intermediate ions in solutions of uni-bivalent salts, the solubility product as calculated becomes much more constant. Fig. 2 indicates that the solubility product of a bi-bivalent salt, calculated on the *usual assumption* that intermediate and complex ions are absent, increases with extreme rapidity as the concentration of the solution (the total ion concentration) increases. Thus, when copper sulfate is the added salt, the solu-

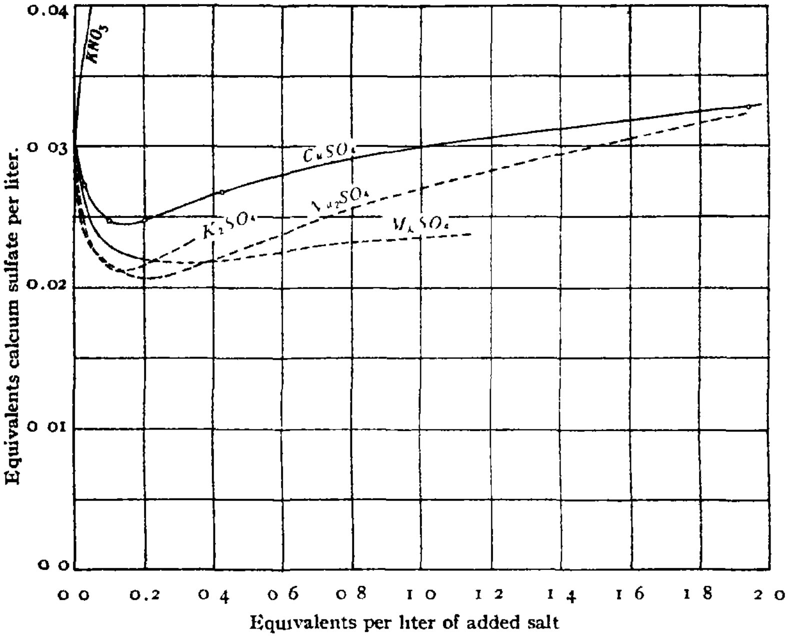


Fig 1 —Solubility of calcium sulfate in solutions of other salts Note that the solubility *decrease* when the concentration of the added salt is only 0 1 equivalents is very much less than corresponds to the solubility-product principle At higher concentrations the curves take on the form of *non-common* ion curves

bility product is increased to more than 3 times its smallest value before the total ion concentration has reached 0.1 *N*, so the apparent activity of the bivalent ions *decreases very rapidly* with increasing ion concentration. It is, of course, possible that the *whole* of such a very rapid increase in the solubility product of salts of this class, cannot be explained by the assumption of the existence of complex ions.

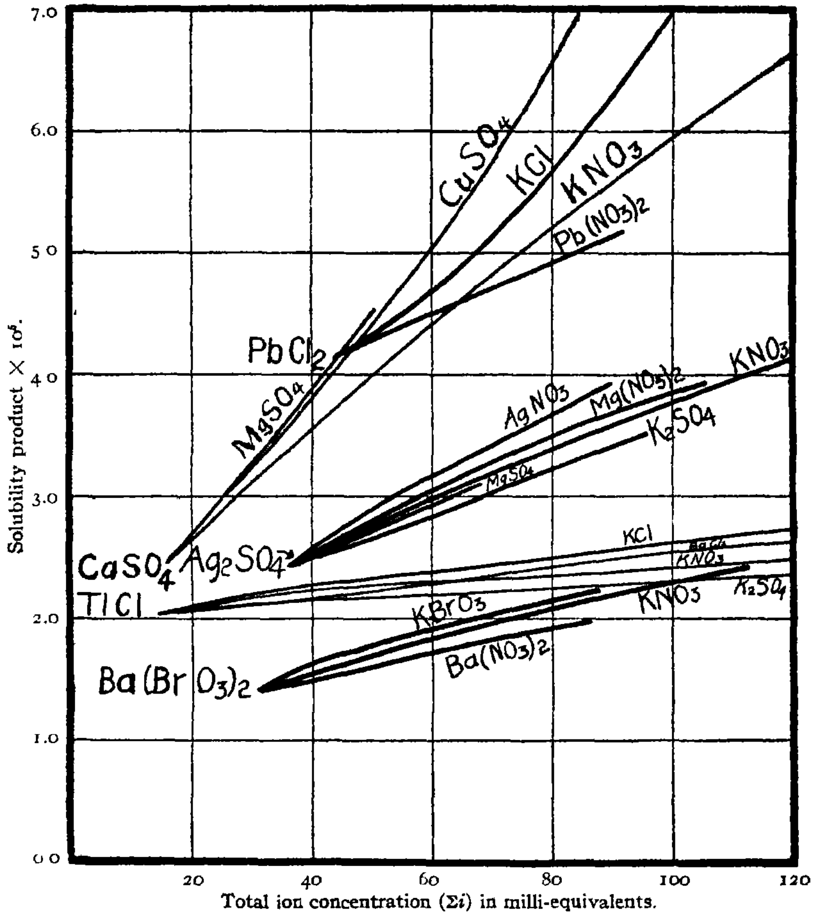


Fig 2.—The solubility product for uni-univalent, uni-bivalent, and bi-bivalent salts, calculated on the assumption that intermediate ions are absent.

The solubility of the un-ionized part of the salt as calculated on the assumption that intermediate ions and other complexes are absent (Fig. 3) is much more constant than it was found to be for uni-uni- and uni-bivalent salts, except in the more concentrated solutions in which copper sulfate is the added salt. The change in the slope of these curves as compared with those for the uni-univalent salts, is in the same direction as that for uni-bivalent salts when the common bivalent ion is added, that is the change in slope is in the direction to be expected if intermediate ions are present.

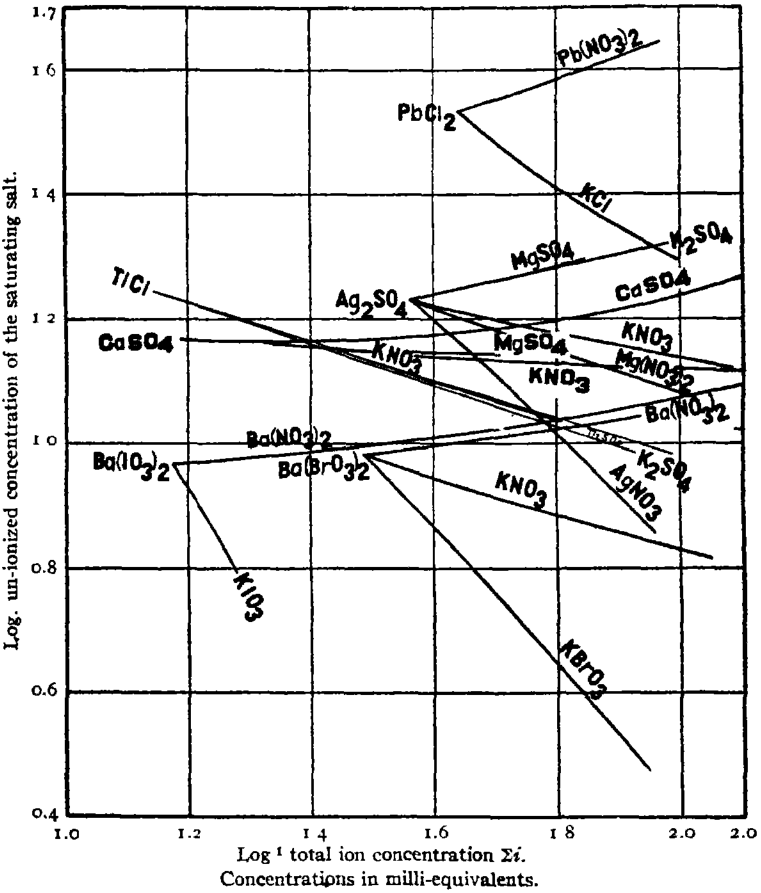


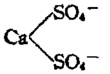
Fig. 3.—The concentration of the un-ionized part of uni-univalent (TlCl), uni-bivalent ($Ba(IO_3)_2$, $Ba(BrO_3)_2$, Ag_2SO_4, $PbCl_2$) and bi-bivalent ($CaSO_4$) salts in their saturated solutions in the presence of other salts, calculated on the incorrect consumption that intermediate ions are absent.

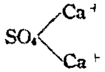
---

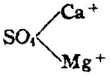
[1] The curves for *barium iodate* should be *ten squares lower down* and *five squares further to the left.* Note how closely these curves parallel those for barium bromate in spite of their large displacement.

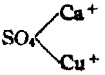
It is to be *specially noted that most of the results described above were obtained in dilute solutions*, that is below 0.1 N total ion concentration, and that therefore they are not to be considered from the standpoint of much of the work in the literature in regard to the formation of double or complex salts in concentrated solutions. The formation of these latter double and complex salts is highly specific, while that for which evidence is obtained in this paper will undoubtedly be found to be general, just as the similar behavior of uni-bivalent salts described in the first paper of this series, was later proved to be perfectly general.

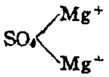
As has been suggested in the first part of this paper, a large part of this abnormal behavior of bi-bivalent salts would be only apparent if complex bivalent ions are formed. These would have the form

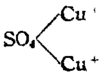


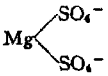


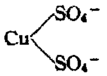


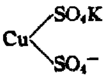




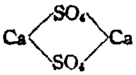


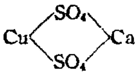


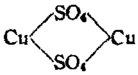


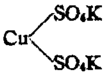


and would form salts of a ring structure:









etc.

Since the formation of such intermediate ions or ring or double salts stores the materials in forms in which they do not enter into the primary equilibrium between the solid, the un-ionized part of the salt consisting of single molecules, and the ordinary ions,[1] it increases what is called the solubility of the salt by approximately the amount of the material put into such forms. This is similar to the increase in the solubility of a salt by metathesis. The complex ions do not enter into the simple solubility product equilibrium, as it actually is, but since they carry the current, they make the apparent number of simple ions greater than accords with the facts, so that the solubility product calculated on the basis of the apparent number instead of the real number of simple ions, comes out too large, and since the number of intermediate ions increases rapidly with the concentration, the apparent solubility product, also increases very rapidly.

The equivalent solubility S_o of a salt which dissociates in the above manner may be given as follows:

$$S_o = 2(AB)_o + 4(A_2B_2)_o + 2(B_o) + 2(ABA)_o + 4(BAB)_o,$$

where AB represents the number of mols of the un-ionized single molecules, A_2B_2 of the double molecules, B of the positive ion, ABA of the negative intermediate ion, and BAB of the positive intermediate ion. A more complete analysis for the similar case of a uni-bivalent salt has already been given in a former paper of this series.[1]

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[1] When this series of researches was begun in 1910 it was the intention to investigate complex formation in salts of the uni-univalent type. Since that time this problem has been taken up by G McP Smith and his students in a series of comprehensive studies. See THIS JOURNAL, 40, 1802 (1918).

In solutions of uni-bivalent salts, in addition to intermediate ions such as KSO_4^-, ions of the type of $K-SO_4-SO_4^-$ are to be expected, while in concentrated solutions of uni-univalent salts, there is much probability that double molecules such as K_2Cl_2, and their complex or intermediate ions, K_2Cl^+ and KCl_2^- exist.[1]

While the evidence for the existence of complex ions in solutions of bi-bivalent salts is neither so complete or so perfect as that obtained in solutions of uni-bivalent salts from the standpoint of the solubility results obtained thus far, there is an independent line of evidence which could not be obtained in the latter case; that is the mobility of the ions in bi-bivalent salt solutions decreases rapidly as the concentration of the solution increases. This change is in the direction to be expected if complex ions are present. Such complex ions differ from the complex ions usually considered in the literature in that the evidence points to their existence in dilute solutions, just as is the case with intermediate ions. In this respect the complex ions considered in this paper are more like such intermediate ions; and so might well be called intermediate ions, since they are intermediate between the single and the double molecules of the salt.

Summary.

1. It has been shown in former papers by Harkins and his co-workers that salts of the tri-ionic and still higher types ionize in steps and give, even in 0 1 or 0 1 N solutions, a very considerable percentage of intermediate ions. The present paper shows that the solubility relations of calcium sulfate when common ions are added, are very similar to those of such higher type salts. This indicates the probability that complex ions, such as $Ca(SO_4)_2^{--}$ and $Ca_2SO_4^{++}$ are present in the solutions. These complex ions differ from what are usually considered under this designation, since they are present to a considerable extent in dilute solutions, so in this sense they are more like intermediate ions.

2. If it is assumed that such complex ions are absent, the solubility prod-

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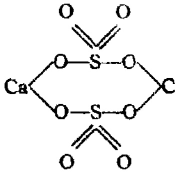
[1] According to the octet theory of Lewis, lately amplified by Langmuir, these salts would have the structure  where each bond represents a pair of electrons, common to two octets.

uct calculated on this basis is found to increase with great rapidity as the concentration increases; thus, if the total ion concentration increases from 0.02 to 0.10 *N* the solubility product is tripled, so, if only simple ions are present their activity decreases very rapidly with an increase in concentration. On the other hand, the solubility found for the un-ionized part on the basis of this assumption, remains much more constant than in the case of uni-univalent salts. The change in the slope of these curves is in the direction which is to be expected if complex ions are present.

3. The percentage concentration of such complexes is much higher in copper sulfate than in magnesium sulfate solutions, at the lower concentrations.

CHICAGO, ILLINOIS.

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF THE GENERAL ELECTRIC CO.]

A NEW METHOD OF CHEMICAL ANALYSIS.

BY A. W. HULL.

Received April 16, 1919.

Two methods of X-ray chemical analysis are already fairly well known.

The first, which may be called X-ray spectrum analysis, is the result of the classical experiments of Moseley,[1] and consists in attaching the substance to be investigated to the target of an X-ray tube and photographing its X-ray line spectrum. The X lines belonging to each element are very few in number as compared with the very large number in the visible spectrum, and they bear a simple relation to the atomic numbers of the elements, so that they can be identified quickly and absolutely by comparison with standard tables. Moseley's measurements have been extended by Siegbahn[2] and his collaborators to practically all known elements of atomic weight greater than sodium, and the lines have been collected in a table for convenient reference.[2] This method is applicable to all substances which can be attached to the target of an X-ray tube, except those in the first row of the periodic table.[3] It thus supplements visible spectrum analysis in being most easily applicable where the latter is least so, *viz.*, to substances not easily volatilized.

The second method, which may be called the X-ray absorption band method, is due to the discovery by Barkla[4] of the X-ray absorption bands of the chemical elements. The position of the edges of these bands have now been measured accurately and tabulated for practically all the elements above zinc[1] by Duane and Blake. The method of analysis consists in placing the substance to be examined, in the form of an absorbing layer, either liquid or solid, in front of an X-ray tube, photographing the spectrum, and comparing the absorption bands in the photograph with the tabulated values. It is applicable to all chemical elements except those in the first row of the periodic table.

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[1] Moseley, *Phil. Mag.*, 26, 1024 (1913); 27, 703 (1914).

[2] Siegbahn, *Jahrb. Radioact. Electronik.*, 13, 336 (1916).

[3] The limitation is due to the fact that no crystal is known with atoms far enough apart to act as a grating for the relatively long wave lengths charaeteristic of these first row elements.

[4] *Phil. Mag.*, 17, 739 (1909).

Both of these methods give evidence only of the chemical elements present, and not of their state of chemical combination. Both are capable of quantitative as well as qualitative application. They have the advantage over older methods that their results are absolutely unambiguous, since they depend only on the atomic numbers of the elements in question, and not upon any of their chemical properties or states of combination. The fact that these methods have not as yet come into common use is due not so much to any difficulty in their application, as to the fact that they are new, and that no problem of sufficient importance has presented itself to warrant their rapid development.

The purpose of this paper is to describe a third and fundamentally different method of X-ray chemical analysis. It is simpler than the other two in that it does not require a spectrometer, and it supplements them in that it gives evidence which they do not supply, namely, the state of chemical combination for each of the elements present.

The method consists in reducing to powder form the substance to be examined, placing it in a small glass tube, sending a beam of monochromatic X-rays through it, and photographing the diffraction pattern produced. The only apparatus required is a source of voltage, an X-ray tube, and a photographic plate or film. The amount of material necessary for a determination is one cubic millimeter. The method is applicable to all chemical elements and compounds which are crystalline in structure.[2]

The arrangement of apparatus is shown in Fig. 1. T is a transformer furnished with an extra coil for lighting the filament of the X-ray tube; X a Coolidge X-ray tube; F a sheet of metal, properly chosen,[3] serving as a filter; S_1 and S_2 slits in thin sheets of lead; T a thin-walled tube, about one mm. in diameter, of some light amorphous material, such as glass, celluloid, or collodion, containing the powdered substance to be tested;

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[1] *Phys. Rev.*, 10, 697 (1917).

[2] The number of non-crystalline solid substances is probably very small. All the solids thus far examined, including many that have been considered amorphous, have been found crystalline with the single exception of glass.

[3] The filter is chosen of such material that it specially absorbs all wave lengths shorter than the desired one, leaving practically nothing but a single intense line, the α line of the K series of the anode material. The proper material for the filter depends upon the material of the X-ray tube anode. For a molybdenum X-ray tube the proper material is zirconium. For details see *Phys. Rev.*, 10, 665 (1917).

and F a narrow strip of photographic film bent over a semicircular strip of brass or wood, concentric with T.[1]

The rays from the X-ray tube pass first through the filter, which absorbs all but a single wave length; then through the two slits, which confine them to a narrow beam (about one mm. wide); then through the powdered material, which scatters or "reflects" a very small fraction of them; and thence to the center of the photographic film. An exposure of one hour will generally give all the information desired.

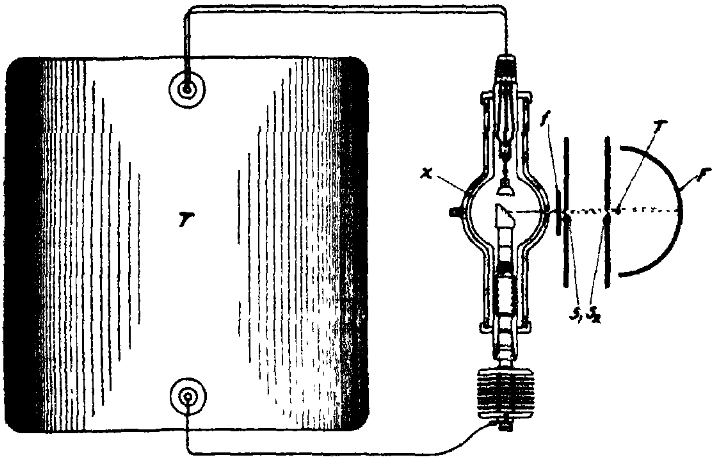

Fig. 1.

When the film is developed it shows, in addition to the over-exposed line in the center, where the direct beam strikes, a series of other lines on each side of the center. These lines are caused by the "reflections" of the X-rays from the tiny crystals in the powder. Their distance from the center of the film depends on the distance between the planes of atoms in the crystal, and there is one line for every important set of planes in the crystal. It is evident, therefore, that substances with different crystalline structure will give entirely different patterns of lines (compare, for example, silicon, magnesium oxide, lithium fluoride, Fig. 4). Substances of similar chemical nature, on the other hand, will in general

Fig. 2.

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[1] For rapid work it is desirable to use *Dupli-Tized* X-ray film, and place on each side of it a thin strip of calcium tungstate intensifying screen.

have similar crystal structure, and give similar patterns, so that it is often possible to identify a photograph at a glance as belonging to a certain type of element or compound. Thus, lithium, sodium and potassium fluorides, sodium and potassium chlorides, and magnesium oxide (Fig. 3) all have the same arrangement of atoms in their crystals, and all give precisely similar patterns of lines, the one being simply a magnified image of the other. The magnification or spread of the pattern is different for each one, being inversely proportional to the cube root of the molecular volume. Since no two similar substances have *exactly* the same molecular volume, it is easy to distinguish them, as the difference is cumulative for lines far from the center.[1] As an example, the photographs of potassium and sodium chlorides which are the nearest together of any of the patterns thus far investigated, have been placed side by side in Fig. 3 for comparison. A further distinguishing mark is the relative intensity of the different lines, which differs greatly even in the most closely related compounds, depending on the relative shapes and sizes of the atoms in the compound. Thus lithium fluoride, magnesium oxide, sodium fluoride and potassium chloride have precisely similar patterns (Fig. 3), but certain lines, as the first and fourth, are very strong in lithium fluoride,

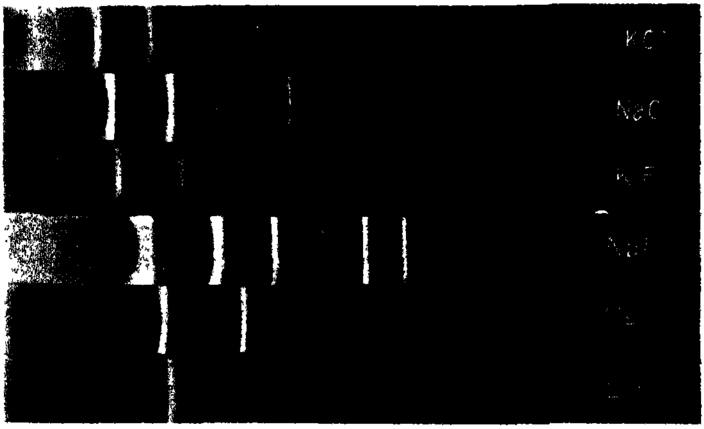

Fig. 3.

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[1] The lines farthest from the center diverge even more than the difference in molecular volume, since the cube root of molecular volume is strictly proportional, inversely, to the *sine* of the angles of reflection, whereas the distances of the lines from the center are proportional to the angles themselves. The difference is negligible for lines near the center (small angles), but for large angles the dispersion thus produced is very large, so that two exactly similar substances differing in molecular volume by less than 1% could easily be distinguished.

fairly strong in magnesium oxide, barely visible in sodium fluoride, and entirely lacking in potassium chloride.

Further details concerning the theory of the production of these lines, and their relation to the crystalline structure of the substance, will be found in the *Physical Review*.[1] This theory will not be reproduced here, as it is not essential to chemical analysis, beyond establishing the facts that every crystalline substance gives a pattern; that the same substance always gives the same pattern; and that in a mixture of substances each produces its pattern independently of the others, so that the photograph obtained with a mixture is the superimposed sum of the photographs that would be obtained by exposing each of the components separately for the same length of time. This law applies quantitatively to the intensities of the lines, as well as to their positions, so that the method is capable of development as a quantitative analysis.

As illustrations of the general type of photographs obtained with simple compounds and elements, Fig. 2 shows two typical photographs, of silicon and sodium fluoride, respectively; Fig. 3 a series of isomorphous alkali halogens, illustrating their similarity of pattern and their differences in spacing and intensity; and Fig. 4 gives a series of dissimilar substances, illustrating their different types of pattern.

Fig. 4.

As practical examples, two actual analyses will be described. They are only roughly quantitative, but could easily be refined to any required accuracy. In addition, they give information which no other method of analysis can furnish.

The first analysis was of a sample of sodium fluoride, taken from stock, labelled "C. P." It was photographed in the manner described and gave the pattern shown in the middle section of Fig. 5. A sample of very pure sodium fluoride was then prepared and photographed, with the results shown in the lower section of Fig. 5. It is evident from the correspondence of the lines that the unknown sample was sodium fluoride, but that it contained a large amount of impurity, which one would estimate, from the relative intensity of the lines, at 30 or 40%.[1] In order to determine

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[1] *Phys. Rev.*, 10, 661–696 (1917).

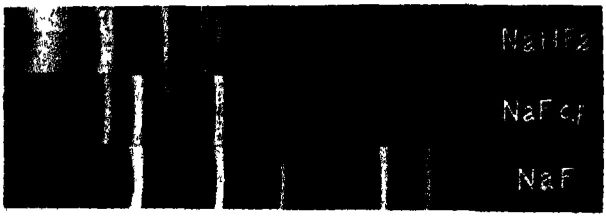

Fig. 5.

the nature of the impurity, a series of photographs was taken of substances which were considered the most probable constituents, such as sodium carbonate, sodium chloride, sodium hydrogen fluoride, etc. The pattern of sodium hydrogen fluoride is shown in the upper section of Fig. 5. It is evident at a glance that it corresponds to the impurity in the test sample of sodium fluoride, and a careful examination shows that all the lines not common to the two lower photographs are common to the two upper ones. In other words, sodium hydrogen fluoride is the only impurity that is present in appreciable quantity. The amount present can be roughly estimated from the relative intensity of the lines, and this could be made into a quantitative method by preparing for comparison a series of photographs of mixtures of known composition.

The fact to be emphasized, however, is that this analysis shows that the sample consisted of a simple mixture of separate crystals of sodium fluoride and sodium hydrogen fluoride, and not a mixture of these with a hydrate, or some more complex compound. Information of this kind might, in some cases, be of considerable value, and it can always be obtained by this method.

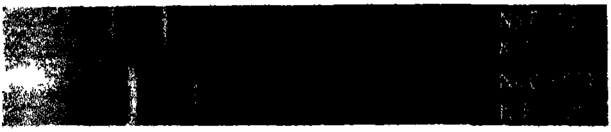

Fig 6.

The second example is the analysis of two samples of identical chemical content, *viz.*, 33.5% potassium, 19.7% sodium, 16.3% fluorine, and 30.5% chlorine. The photographs given by these two samples are shown together, for comparison, in Fig. 6. It is evident that the two samples are far from being identical, in fact, that they contain nothing in common.

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[1] This sample was later titrated and found to contain 19.2% F, which corresponds to 60% $NaHF_2$.

The first of these photographs is shown again in Fig. 7, in comparison with sodium fluoride and potassium chloride, and is seen to contain all the lines of both of them, and no other lines. Hence this sample consists of a mixture of sodium fluoride and potassium chloride (36% sodium fluoride, 64% potassium chloride) and nothing else. To show how conclusive the test is, this same sample is shown again in Fig. 8 in comparison with sodium chloride and potassium fluoride It is evident that neither of these patterns is present in the sample The chance correspondence of individual lines has no meaning If a substance is present, *its whole pattern* must be present in the photograph, and the relative intensities in this pattern must be the same as in the comparison standard. Thus the absence in the test photograph of a *single* intense line of any comparison

Fig 7

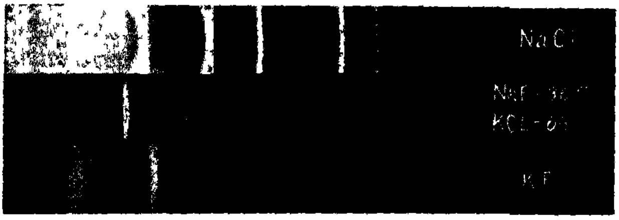

Fig 8

Fig. 9.

substance proves that *none* of this substance is present, and that any other correspondences between the two are mere chance.

The second sample is shown in Fig. 9, in comparison with sodium chloride and potassium fluoride, and it is evident that it consists of a mixture of these two salts (50.2% sodium chloride, 49.8% potassium fluoride) and *nothing else.*

These examples are very simple ones. It is possible to go much further. By narrowing the slits and using a smaller tube of test material very sharp, narrow lines can be obtained, and a mixture of several substances analyzed without ambiguity. Furthermore, by long exposures, so as to greatly overexpose the principal components of a mixture, substances present only in very small amounts can be made to show.

SCHENECTADY, N. Y.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIV. OF CALIFORNIA.]

THE APPLICABILITY OF THE PRECIPITATED SILVER-SILVER CHLORIDE ELECTRODE TO THE MEASUREMENT OF THE ACTIVITY OF HYDROCHLORIC ACID IN EXTREMELY DILUTE SOLUTIONS.

BY G. A. LINHART.

Received May 21, 1919

A study of the hydrogen and silver-silver chloride electrodes in aqueous hydrochloric acid has received much attention in recent years and the subject has been reviewed in several articles of recent date.[1]

In all previous investigations, however, measurements in solutions as dilute as 0.01 *M* have been subject to slight uncertainty, and at higher dilutions they have proved unreliable. By using a cell of new design capable of holding a large amount of the electrolyte, by taking extraordinary care in the preparation of the materials, and by replacing the customary electrode of silver, covered with chloride through electrolysis, by a mass of finely divided silver in intimate contact with silver chloride, precipitated metathetically, it has proved possible to obtain results of high precision nearly to a concentration of 0.0001 *M*, as described below.

The Preparation of Materials.

The *silver* was deposited by a current of 5 to 7 amperes in a cell consisting of an anode of silver and a cathode of fine platinum wire, dipping into a solution of silver nitrate. Under the influence of this large current the silver gathered about the platinum wire in loose, spongy clots, easily loosened by a light tapping of the wire. The silver so obtained was then washed (the water used throughout this investigation was prepared by redistilling distilled water with alkaline permanganate) and kept under pure water until needed. The *silver chloride* was prepared from purified silver nitrate and hydrochloric acid and preserved in the dark under pure water, remaining white indefinitely.

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[1] Lewis, Brighton and Sebastian, THIS JOURNAL, 39, 2245 (1917); Noyes and Ellis, *Ibid.*, 39, 2539 (1917).

Description of the Apparatus.

In the cell represented by Fig. 1,[1] the hydrogen gas passes through the bubbler in the direction indicated by the arrows, enters the cell *via* the pin holes above the silver chloride, rises through the solution up to the iridized plate, and then passes out through the trap. The silver-silver chloride electrode is shown at the bottom of the apparatus and is connected to a lead wire by a sealed-in platinum wire and the column of mercury shown shaded in the diagram. The hydrogen electrode is connected with its terminal wire in similar manner.

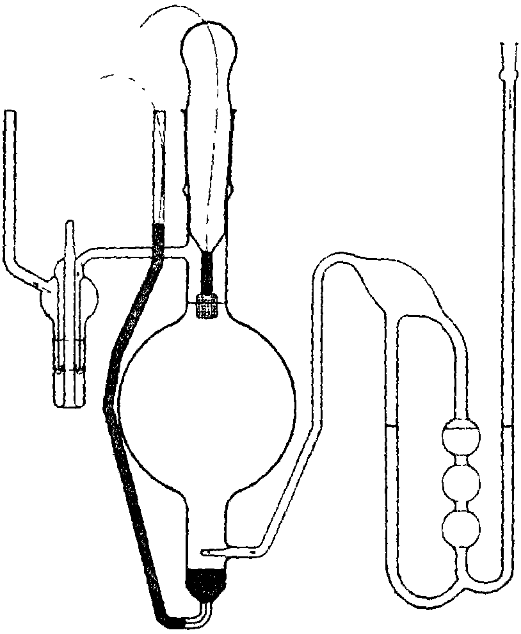

Fig 1

In order that the hydrogen shall not come in contact with grease, the seat of the glass stoppe is so made that th upper portion of th finely ground surfac may be covered with film of stopcock greas without contaminatin the lower portion of tl ground surface. Tl connection between tl hydrogen generator a the cell is made by ground glass joint instead of the customary glass seal. This modificati has been found more convenient and quite as efficient. The wh apparatus was affixed to a frame of asbestos board in order to elimin the danger of breakage by handling of the glass parts.

The iridized electrode, the hydrogen generator, the electrical apparat and the thermostat were of the types described and figured in a rec article by Lewis, Brighton, and Sebastian.[2]

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[1] This instrument was constructed by Mr. W. J. Cummings of this laborat For the drawing I am indebted to Mr Thomas Fraser Young.

[2] *Loc. cit.*

Experimental Procedure.

Requisite amounts of silver and silver chloride were separately washed many times by decantation with the same hydrochloric acid solution to be used in the cell for any particular experiment. The silver was then placed in the bottom of the cell to the depth indicated in the figure and covered with a layer of silver chloride. The whole cell was now filled with the hydrochloric acid to the levels indicated in the figure. The bulb of the cell measured about 1200 cc.

The whole apparatus was then connected, immersed in an oil thermostat, kept at 25° ± 0.01°, and allowed to come to equilibrium. This usually took from 3 to 4 days, depending upon the concentration of the acid, before the e. m. f. became reasonably constant In Table I are given all the recorded readings and in Table II only those after the e. m. f. had become constant. The table headings are self-explanatory. All concentrations are expressed in mols per 1000 grams of water.

TABLE I —RECORDED READINGS

(a)		(c).	
$\Sigma(HCl)$ = 0.04826		$\Sigma(HCl)$ = 0.004826.	
E m f	Time in hours	E m f	Time in hours.
0.3799	12	0.4910	12
0.3823	16	0.4954	16
0.3842	21	0.4965	18
0.3853	26	0.4978	21
0.3864	36	0.4988	26
0.3866	40	0.4996	35
0.3868	46	0.4997	39
0.3869	50	0.4998	43
0.3870	61	0.4998	48
0.3870	64	0.4998	61
0.3870	68	..	...

(b)		(d).	
$\Sigma(HCl)$ = 0.00965		$\Sigma(HCl)$ = 0.001000.	
E m f	Time in hours	E m. f	Time in hours
0.4622	24	0.5698	19
0.4625	25	0.5716	22
0.4634	29	0.5769	43
0.4642	33	0.5775	51
0.4650	44	0.5778	56
0.4651	48	0.5781	66
0.4653	53	0.5783	74
0.4653	58	0.5784	79
0.4654	68	0.5785	91
0.4654	72	0.5786	103
0.4654	78	0.5786	114
		0.5786	127
.	.	0.5786	139
		0.5787	149
	...	0.5787	192
.	...	0.5787	200

redistilling distilled water with alkaline permanganate) and kept under pure water until needed. The *silver chloride* was prepared from purified silver nitrate and hydrochloric acid and preserved in the dark under pure water, remaining white indefinitely.

Description of the Apparatus.

In the cell represented by Fig. 1,[1] the hydrogen gas passes through the bubbler in the direction indicated by the arrows, enters the cell *via* the pin holes above the silver chloride, rises through the solution up to the iridized plate, and then passes out through the trap. The silver-silver chloride electrode is shown at the bottom of the apparatus and is connected to a lead wire by a sealed-in platinum wire and the column of mercury shown shaded in the diagram. The hydrogen electrode is connected with its terminal wire in similar manner.

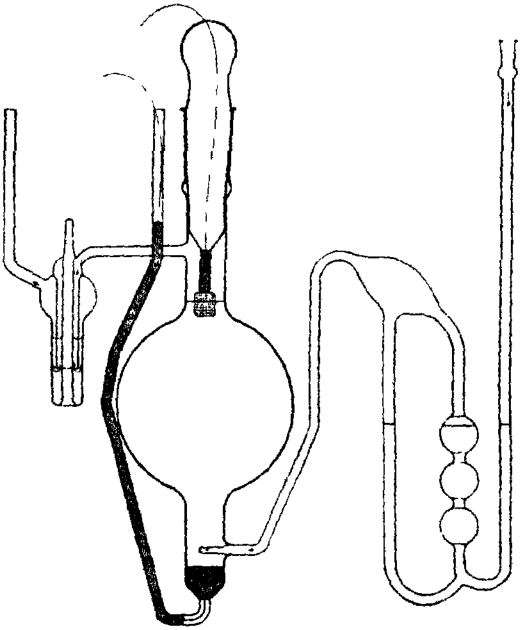
Fig 1

In order that the hydrogen shall not come in contact with grease, the seat of the glass stopper is so made that the upper portion of the finely ground surface may be covered with a film of stopcock grease without contaminating the lower portion of the ground surface. The connection between the hydrogen generator and the cell is made by a ground glass joint instead of the customary glass seal. This modification has been found more convenient and quite as efficient. The whole apparatus was affixed to a frame of asbestos board in order to eliminate the danger of breakage by handling of the glass parts.

The iridized electrode, the hydrogen generator, the electrical apparatus, and the thermostat were of the types described and figured in a recent article by Lewis, Brighton, and Sebastian.[2]

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Experimental Procedure.

Requisite amounts of silver and silver chloride were separately washed many times by decantation with the same hydrochloric acid solution to be used in the cell for any particular experiment. The silver was then placed in the bottom of the cell to the depth indicated in the figure and covered with a layer of silver chloride. The whole cell was now filled with the hydrochloric acid to the levels indicated in the figure. The bulb of the cell measured about 1200 cc.

The whole apparatus was then connected, immersed in an oil thermostat, kept at 25° ± 0.01°, and allowed to come to equilibrium. This usually took from 3 to 4 days, depending upon the concentration of the acid, before the e. m. f. became reasonably constant. In Table I are given all the recorded readings and in Table II only those after the e. m. f. had become constant. The table headings are self-explanatory. All concentrations are expressed in mols per 1000 grams of water.

TABLE I.—RECORDED READINGS

(a)

Σ(HCl) = 0.04826

E. m. f.	Time in hours
0.3799	12
0.3823	16
0.3842	21
0.3853	26
0.3864	36
0.3866	40
0.3868	46
0.3869	50
0.3870	61
0.3870	64
0.3870	68

(b)

Σ(HCl) = 0.00965

E. m. f.	Time in hours
0.4622	24
0.4625	25
0.4634	29
0.4642	33
0.4650	44
0.4651	48
0.4653	53
0.4653	58
0.4654	68
0.4654	72
0.4654	78
..	...

(c)

Σ(HCl) = 0.004826

E. m. f.	Time in hours
0.4910	12
0.4954	16
0.4965	18
0.4978	21
0.4988	26
0.4996	35
0.4997	39
0.4998	43
0.4998	48
0.4998	61
	..

(d).

Σ(HCl) = 0.001000.

E. m. f.	Time in hours
0.5698	19
0.5716	22
0.5769	43
0.5775	51
0.5778	56
0.5781	66
0.5783	74
0.5784	79
0.5785	91
0.5786	103
0.5786	114
0.5786	127
0.5786	139
0.5787	149
0.5787	192
0.5787	200

(*e*).

$\Sigma(HCl) = 0.000483$.

E. m. f.	Time in hours
0.6106	12
0.6121	24
0.6139	38
0.6144	48
0.6149	60
0.6152	70
0.6157	80
0.6157	92
0.6157	104
. .	.
	.
.	.
.	.
. .	. .
. .	
. .	.
. .	
. .	
.	

(*f*).

$\Sigma(HCl) = 0.000242$.

E. m. f.	Time in hours.
0.6556	19
0.6565	21
0.6563	28
0.6549	35
0.6534	43
0.6529	46
0.6519	52
0.6514	58
0.6512	68
0.6511	72
0.6511	77
0.6510	84
0.6509	92
0.6509	96
0.6509	101
0.6509	108
0.6509	116
0.6508	120
0.6509	124

(*g*)

$\Sigma(HCl) = 0.000136$

E. m. f.	Time in hours
0.6899	20
0.6894	24
0.6889	28
0.6872	36
0.6860	45
0.6849	48
0.6833	59
0.6817	69
0.6814	76
0.6809	84
0.6803	96
0.6799	106
0.6797	116
0.6798	126

TABLE II.

Readings after Electromotive Force had Become Constant.

Expt. No	$\Sigma(HCl)$	E. m. f.	E. m. f. calc. to one atmos. H_2	E'	$\frac{\sqrt{(H^+)(Cl^-)}}{\Sigma(HCl)}$	$\frac{(H^+)(Cl^-)}{(HCl)}$
1.....	0.04826	0.3870	0.3874	0.2317	0.8513	0.2342
2......	0.00965	0.4654	0.4658	0.2274	0.9256	0.1111
3......	0.004826	0.4998	0.5002	0.2262	0.9475	0.0825
4......	0.001000	0.5787	0.5791	0.2242	0.9845	0.0626
5......	0.000483	0.6157	0.6161	0.2238	0.9920	0.0594
6......	0.000242	0.6509	0.6514	0.2236	0.9960	0.0600
7......	0.000136	(0.6798)	(0.6805)	(0.2231)	. .	. . .

At extreme dilution, $E' = 0.2234 = E^\circ$.

Discussion of Results and Conclusion.

Concerning the solubility of silver chloride at 25° only 3 values are to be found in the literature,[1] all based on conductivity measurements, namely: $1.60(10)^{-5}$, $1.64(10)^{-5}$, $1.41(10)^{-5}$; average $1.55(10)^{-5}$, and the product $2.4(10)^{-10}$. Dividing this value by the concentration of Expt. 6 gives 0.0000010, or 0.4%, corresponding to 0.1 mv.; divided by the concentration of Expt. 7 gives 0.0000018, or 1.3%, corresponding to 0.3 mv. In the other experiments the correction becomes entirely negligible. In the third column of the above table the last two numbers have been so corrected for the solubility of silver chloride. The fourth column gives *E'*, the e. m. f. calculated to molal concentrations of the hydrogen ions and chloride ions on the assumption of 100% dissociation at each concentration. The extrapolation of this number to infinite dilution gives *E°*, the standard e. m. f. at hypothetical molal concentration of the ions. With this value the thermodynamic or "corrected" degree of dissociation at each concentration is obtained by familiar methods and given in the 5th column of the table above.

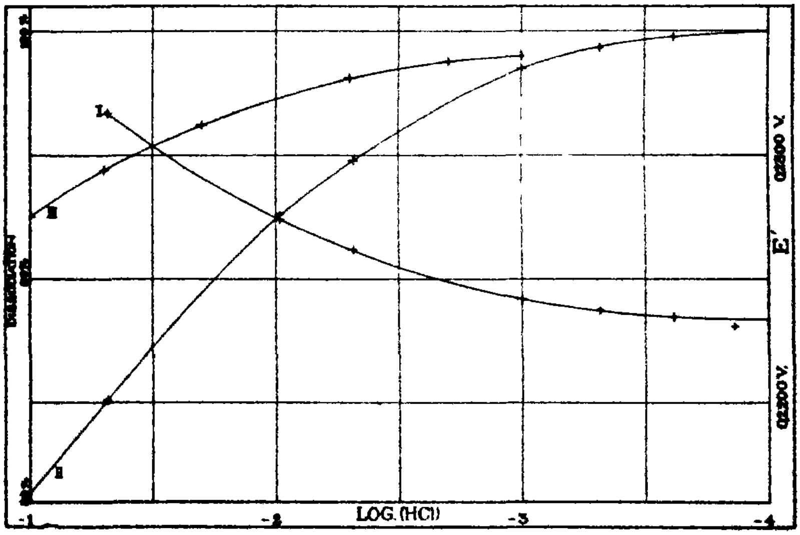

Fig 2.

In Fig. 2, Curve I gives the values of *E'*. Judging from the trend of the curve the last value (Expt. 7) is probably 0.3 mv. too low, owing to the uncertainty of the concentration of the (HCl) to the extent of several tenths of a per cent., and also to the questionable solubility product of the silver chloride. Curve II gives the calculated degrees of dissociation, and, for comparison, Curve III gives the degrees of dissociation as measured by conductivity methods.[1]

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[1] Thiel, *Z. anorg. Chem.*, 24, 57 (1900).

NOTE.—In a private communication Professor Loomis informs me that a statement in regard to his work in one of my articles (THIS JOURNAL, 39, 2604 (1917)) is rather ambiguous: "The remark might be interpreted to intimate that I have claimed equal thermodynamic degrees of dissociation for KCl and HCl solutions at all concentrations. As a matter of fact my articles have dealt only with decinormal concentrations, and in my latest article I have suggested a possibility that my results may be accounted for by a slightly lower degree of dissociation for 0.1 *N* KCl than for 0.1 *N* HCl."

BERKELEY, CAL.

[CONTRIBUTION FROM CHEMICAL LABORATORY, EDGEWOOD ARSENAL.]

A MODIFIED METHOD FOR THE ANALYSIS OF MIXTURES OF ETHYLENE AND ACETYLENE.[2]

BY WILLIAM H. ROSS AND HARLAN L. TRUMBULL.

Received May 23, 1919.

In the course of an investigation on the preparation of ethylene from acetylene, mixtures of these two gases were recovered in association with variable quantities of other gases as ethane and hydrogen. It thus became necessary in carrying on the work to make accurate analyses of gas samples containing ethylene in the presence of acetylene and other hydrocarbons in order to determine the effect on the production of ethylene of any special change in the conditions of the experiment.

In the preliminary work use was made of the Tucker and Moody[3] method for determining ethylene in the presence of acetylene. This method involves the use of an ammoniacal silver nitrate solution which is claimed to remove the acetylene completely but only a relatively small amount of ethylene. It was found, however, that the quantity of ethylene absorbed varied with the time that the mixture was shaken with the silver nitrate solution, and that the results obtained varied continuously with the time taken in making an analysis. This was demonstrated by shaking samples of 80% ethylene, known to be free from acetylene, with the silver nitrate solution for 5-minute periods, and reading the residual volume of gas after each period. The results are given in Table I.

In a number of tests made with known mixtures of ethylene and acetylene, note was made of the relative proportion of each absorbed when the mixture of gas was shaken with the silver nitrate solution for different lengths of time. It was thought that tolerably good results might possibly be obtained in the analysis of unknown mixtures if the gas were shaken in the silver nitrate pipet for the same length of time as that which gave best results with the known mixtures. This might possibly prove true in case the mixtures remained approximately of the same composition, and the strength of the silver nitrate solution remained constant. As these factors changed, however, the accuracy of the method was found to range between such wide limits as to make its use unsuited for the accurate analysis of ethylene-acetylene mixtures, particularly when the mixtures contained relatively small amounts of one or the other of these constituents.

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[1] Noyes and Falk, THIS JOURNAL, 34, 475 (1912).

[2] Published by permission of the Director of the Chemical Warfare Service.

[3] THIS JOURNAL, 23, 671 (1901); Dennis', *Gas Analysis*, p. 248.

TABLE I.—ABSORPTION OF ETHYLENE IN AMMONIACAL 2% SILVER NITRATE SOLUTION

Time of shaking Min	Volume of residual gas Sample No 1 Cc	Sample No 2 Cc
0	99.2	100.0
5	93.8	95.0
10	90.6	92.8
15	88.6	90.4
20	86.4	88.0
25	83.6	85.6
30	82.2	83.0
35	80.0	81.0
40	78.6	78.6
45	76.4	76.4
50	75.0	74.6
55	72.2	72.0
60	70.4	70.0

A method for determining acetylene gravimetrically has been suggested by Hempel, which consists in absorbing the gas in ammoniacal cuprous chloride solution with which the acetylene reacts to form a precipitate of copper acetylide. From the weight of copper in the precipitate, which may be determined by any one of several methods, the percentage of acetylene in the sample is then calculated[1] This method is claimed to give accurate results, but was found to be unsuitable for our work on account of the time taken in making an analysis.[2]

Experiments were then undertaken to determine the limits of accuracy of a volumetric method outlined by Chavastelon[3] for the determination of acetylene in gaseous mixtures. It is known that when an excess of acetylene is passed into an ammoniacal solution of silver nitrate a precipitate is formed of the composition C_2Ag_2.[4] When the solution is neutral, however, and the silver nitrate is in excess, the precipitate then has the composition $C_2Ag_2\,AgNO_3$,[3] and a definite proportion of nitric acid is set free in the reaction as represented by the equation

$$C_2H_2 + 3AgNO_3 = C_2Ag_2.AgNO_3 + 2HNO_3.$$

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[1] J. Scheiber, *Z anal. Chem*, 48, 529 (1908)

[2] S A. Tucker and H. R. Moody, THIS JOURNAL, 23, 672 (1901)

[3] *Compt. rend.*, 125, 245 (1897)

[4] E. H. Keiser, *Am. Chem. J.*, 14, 286 (1892); R. Chavastelon, *Compt rend*, 124, 1364 (1897); G. Arth, *Ibid.*, 124, 1534 (1897)

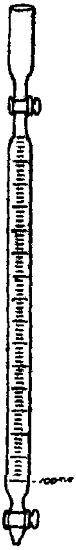

Fig. 1.

This reaction has accordingly been suggested by Chavastelon as the basis of a method for determining acetylene by simply titrating the acidity of the solution recovered when a known volume of gas, free from acid constituents, was absorbed in a solution of silver nitrate. The gas holder devised by Raoult,[1] and represented in Fig. 1, was recommended as the most suitable for use in this determination. When the volume of the sample was sufficiently great the holder was filled by displacement of the air with the sample. With a smaller sample it was suggested that this might be collected directly in the holder over mercury, or by passing it into the holder after the latter had been evacuated. An excess of 10% silver nitrate solution was then placed in the funnel of the gas holder and introduced into the holder where it was shaken until absorption of the gas was complete. The acidity of the resulting solution was then determined by titration and it was held that from the data thus obtained and knowing the volume, temperature and pressure of the gas sample taken, the percentage of acetylene present could then be readily calculated. No further details were given for carrying out the analysis or for making the calculations, and no results of analysis were listed to show the limits of accuracy of the method.

Development of the Method.

When undertaking analyses of gas samples by the method as thus outlined, use was made of the gas holder represented in Fig 2. Each holder had a capacity of about 45 cc., and was provided with a water jacket to prevent the inclosed gas from undergoing the sudden changes in temperature which were found to occur when no jacket was used.

Since acetylene is soluble in water to the extent of 1.1 volume per volume of water at ordinary temperature, and since the use of water requires that a factor be applied to correct for the pressure of water vapor, it was decided to avoid both complications by collecting the samples over mercury. This was contained in the graduated tube A, Fig. 2, which was connected with the gas holder C by means of the rubber tube B. The holder was filled with mercury by opening the stopcocks and lowering it to the proper level. A sample of gas was collected by displacing the mercury into the graduated tube again,

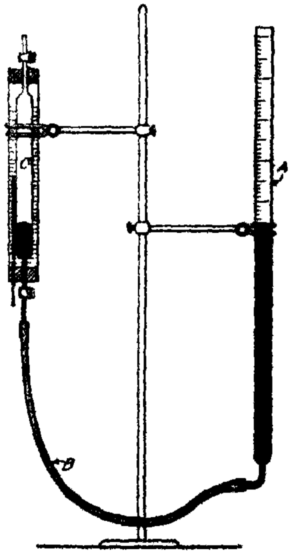

Fig. 2.

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[1] *Compt. rend.*, 82, 844 (1876).

and closing the lower stopcock. The upper stopcock was not closed until the gas was passed into the holder under slightly increased pressure. The holder was then removed from its connection with the graduated tube and allowed to stand until the gas had reached temperature equilibrium. One of the stopcocks was then opened for an instant to bring the gas to normal pressure. C was finally connected to the lower end of a two-foot column of a 5% silver nitrate solution and an excess of the solution then added and shaken up with the gas in the holder until absorption was complete. In the preliminary experiments a 10% solution was used as suggested by Chavastelon, but the less concentrated solution proved the more satisfactory. The solution containing the precipitated silver acetylide was finally transferred to a beaker and titrated with standard sodium hydroxide solution, using phenolphthalein as indicator. It was found, however, that the end-point of the titration when carried out in the way described was too indefinite to give satisfactory results, since the brown color of silver oxide masked the end-point. Attempts were then made to overcome this difficulty by eliminating the excess of silver ion by precipitation with sodium chloride solution. When this was added before the alkali the result was still unsatisfactory, presumably because it effected a reversal of the reaction between the acetylene and the silver nitrate. It was found, however, that when the standard alkali was first added in excess, and the silver then precipitated with sodium chloride, the excess of alkali could be titrated to a very sharp end-point with standard hydrochloric acid solution. When making a titration with this modification, the standard alkali was added until the brown color of silver oxide appeared; the excess of silver in solution was precipitated with about 5 cc. of neutral 20% sodium chloride solution, and the original acidity of the solution then determined by titrating the excess of alkali with standard acid as already explained.

When the volume of gas available for analysis was less than the capacity of the gas holder, the amount collected was measured by noting the rise of mercury in the graduated tube after the surface of the mercury in each vessel was brought to the same level. The upper stopcock was then closed, and the gas holder raised until all the mercury had passed through the lower stopcock. The latter was then closed, and the analysis completed in the usual way.

The following method was used in calculating the results:

Let V_g = volume of gas holder.
T = absolute temperature, 273°.
T_o = temperature of gas sample when collected.
P = standard pressure, 760 mm.
P_o = barometric pressure at the time the sample was collected.

Then the volume of the sample collected in the gas holder when reduced to standard conditions,

$$V = V_g \times P_o/P \times T/T_o = V_g \times P_o/T_o \times 0.3592.$$

Since acetylene reacts with silver nitrate to give two molecules of nitric acid per molecule of gas taken, it follows that 1 cc. of acetylene reduced to standard conditions is equivalent to 0.893 cc. of 0.1 *N* sodium hydroxide solution; or 1 cc. of 0.1 *N* sodium hydroxide solution is equivalent to 1.120 cc. of acetylene. The number of cc. of 0.1 *N* sodium hydroxide solution required in the titration of any sample multiplied by the factor 1.12 thus gives directly the volume which the acetylene in the sample would occupy under standard conditions, and this volume expressed in terms of the total volume of the sample taken gives directly the percentage of acetylene in the sample. By thus calculating once for all the volume of acetylene under standard conditions to which 1 cc. of the standard alkali is equivalent the necessary calculation for subsequent analyses becomes very much simplified.[1]

To test the accuracy of the method as thus developed analyses were made of the gas from an acetylene cylinder and the results compared with those obtained by absorption in fuming sulfuric acid. The acetone in the acetylene coming from the cylinder was removed by passing the gas through a suitable column of water, and the moisture then removed by means of anhydrous calcium chloride. With the volumetric method, using phenolphthalein as indicator, the results were found to vary in the case of 6 analyses from 97.8% to 100.8% of acetylene with a mean of 98 2%. Analysis of the same gas by the method of absorbing in fuming sulfuric acid gave a mean value of 96 3%. The results obtained by the volumetric method thus not only did not agree very closely among themselves but were over 2% greater on an average than the mean value found by the absorption method.

In order to determine the cause of this disagreement in the results, a number of blank titrations were run using the same proportion of the reagents, acetylene alone being omitted, as were taken for the analysis of the gas from the acetylene cylinder. It was found that the reagents exhibited a decided acidity towards phenolphthalein, and that the extent of the acidity varied with the amount of standard sodium hydroxide solution used in the titration. This is shown by the results given in Table II. In each of the experiments there were used 40 cc of a 5% silver nitrate solution and 5 cc. of a 20% sodium chloride solution with water to make 150 cc.

In the analysis of the acetylene samples already referred to, 40 cc. of the standard alkali was added to the solution containing the silver acetylide precipitate, and the excess of alkali then titrated back with the standard acid. For the analysis in question between 2 and 3 cc. of acid was required. In order to determine the blank that might most closely correspond to these conditions, about 36 cc. of the standard acid was added to the acetylene-free silver nitrate solution, followed by 40 cc. of standard alkali. The solution was then titrated with standard acid again to neutrality as indicated by phenolphthalein. Under these conditions the apparent acidity of the reagents amounted to 0.65 cc. of the 0.1 *N* hydrochloric acid. It was found, however, that when methyl orange was used as the indicator in titrations carried out in the same way the reagents then showed exact neutrality.

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[1] In the analysis of acetylene that is stored or collected over water, the value of the vapor pressure of the water at the temperature of the experiment must be subtracted from the barometric pressure. With this correction the remainder of the calculation is then completed in the usual way.

TABLE II.—VARIATION IN THE APPARENT ACIDITY OF THE REAGENTS USED IN ACETYLENE ANALYSIS WITH THE AMOUNT OF STANDARD ALKALI USED IN THE TITRATION

Expt. No.	0.1 *N* NaOH added Cc.	0.1 *N* HCl required Cc.	Apparent acidity of the reagents in cc. of 0.1 *N* HCl
1	2.00	1.82	0.18
2	5.00	4.80	0.20
3	6.00	5.77	0.23
4	10.00	9.62	0.38
5	40.00	39.05	0.95

An analysis was now made of the acetylene from the same cylinder as before, using first methyl orange as indicator, following which a little more standard alkali was added and the titration with acid repeated with use of phenolphthalein. It was found that when the correction of 0.65 cc. was added to the 0.1 *N* hydrochloric acid titration obtained with phenolphthalein the results as calculated from the values found with this indicator were then in exact agreement with those obtained directly with methyl orange. On applying the same correction in a recalculation of the results already reported for the analysis of the gas from an acetylene cylinder it was found that the mean value for the acetylene in the gas analyzed now amounted to 96.7%, instead of 98.2%, which is in quite close agreement with the value 96.3% found by the absorption method.

It is apparent from the results given in Table II, however, that in the analysis of a gas containing a lower percentage of acetylene a different blank correction would have to be applied when using phenolphthalein. This indicator was accordingly discarded in all subsequent analyses in favor of methyl orange. With the latter indicator the end-point is not quite as sharp as with phenolphthalein but the accuracy of any titration may be readily checked by adding successive portions of the standard alkali and then titrating to neutrality as before with the standard acid.

A number of analyses were now undertaken to ascertain the accuracy of the method in the analysis of mixtures of ethylene and acetylene. Pure ethylene does not give any precipitate with silver nitrate solution, but it was noticed that when samples of this gas were collected in the gas holder over mercury a slight precipitate sometimes occurred with development of a corresponding acid reaction. This was traced to the presence of small droplets of mercury which adhered to the interior walls of the gas holder and which then reacting with the silver nitrate used in the analysis, gave rise to an acid reaction through hydrolysis of the mercury salt formed. With a perfectly clean gas holder any quantity of mercury adhering to the gas holder was too small to have any effect on the analysis, but it was found that any appreciable amount of mercury in the solution to be titrated produced a wide variation in the results.

In order to obviate the danger from contamination with mercury a new apparatus was devised to replace that represented in Fig. 2. This is shown in Fig. 3. B is an ordinary gas buret in which the sample to be analyzed is collected over mercury. The gas bulb D has a capacity of

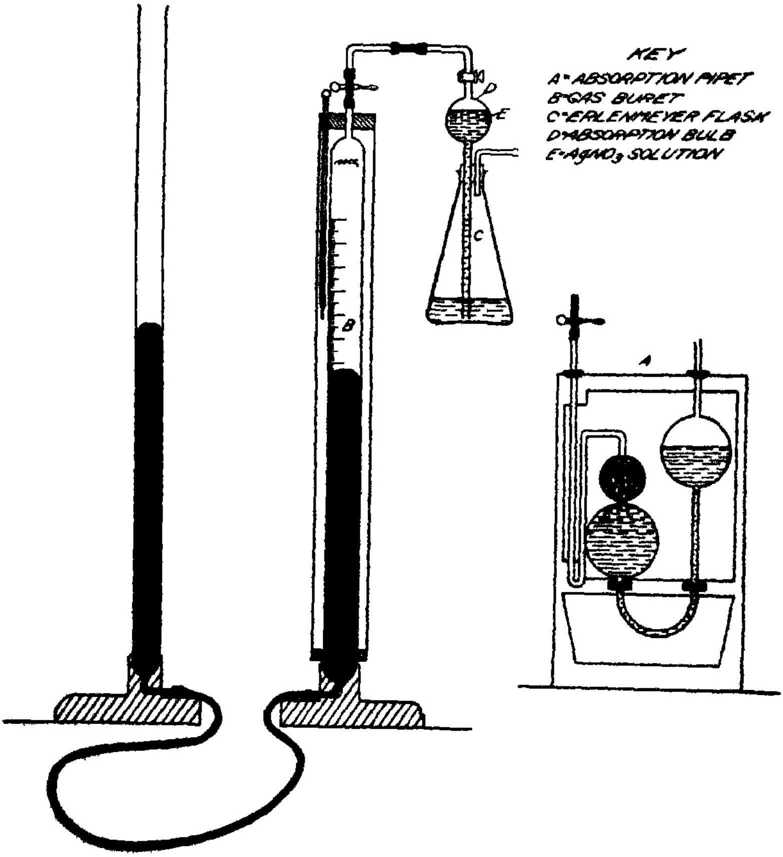

Fig. 3.

about 55 cc. In the Erlenmeyer flask C is placed about 90 cc. of a 2.5% silver nitrate solution. This is then sucked up into the glass bulb and the stopcock at the top closed. Connection is then made with the gas buret as indicated, and about 45 cc. or less of the sample to be analyzed is passed into the bulb over the silver nitrate solution. The stopcock of the glass bulb is then closed, and the latter with its connecting flask disconnected from the buret and shaken until absorption of the gas is complete, or until there is no further rise of the solution into the bulb. The stopcock is then opened, allowing the solution and precipitated silver acetylide to run into the flask. To this is added the rinsings from the bulb, and the titration then made directly in the flask in the usual way.

By use of this procedure for absorbing the gas the occasion for drying a portion of the apparatus before making an analysis, as in the case when a gas holder is used, is avoided, and a further advantage is to be found in the fact that any leak in the apparatus is always inwards so that no loss of the sample takes place.

When testing the accuracy of the method as thus modified in the analysis of ethylene-acetylene mixtures, special precautions were taken to prepare the separate gases free from all other hydrocarbons. The acetylene used was prepared by passing the gas from an acetylene cylinder through water and chromic acid solution, then over solid sodium hydroxide and phosphorus pentoxide and finally through a tube dipped in liquid air. The solid acetylene thus obtained was then allowed to evaporate and the middle portion collected over a 20% sodium chloride solution through which acetylene had abeen allowed to bubble for a time to expel dissolved air. The gas thus collected gave 99.7% absorption in fuming sulfuric acid.

Ethylene of corresponding purity was prepared by dropping ethylene dibromide into an alcoholic solution containing a zinc-copper couple. Known mixtures of the two gases were then made up and analyzed first for acetylene by the volumetric method and then for total ethylene and acetylene by absorption in the fuming sulfuric acid pipet A, Fig. 3. The ethylene percentage was obtained by difference. The results are given in Table III.

TABLE III.—ANALYSIS OF MIXTURES OF ETHYLENE AND ACETYLENE.

Analysis No	% taken			% found		
	Acetylene	Ethylene	Total	Total.	Acetylene.	Ethylene.
1	99.7	0.0	99.7	99.7	99.3	0.0
2	49.9	42.7	92.6	92.3	49.7	42.6
3	28.3	60.4	88.7	87.7	28.0	59.7
4	28.1	60.5	88.6	88.9	28.3	60.6
5	11.8	74.3	86.1	86.1	11.6	74.5
6	10.5	75.6	86.1	86.1	10.3	75.8

In Table IV are given some results which show the agreement to be expected in successive analyses of the same gas by the volumetric method.

The gas to be analyzed was obtained from an acetylene cylinder and purified by passing successively through water, dry calcium chloride, chromic acid deposited on pumice, dry calcium chloride again and finally over sticks of solid potassium hydroxide. Analysis of this gas by the absorption method gave a mean value of 98.1%.

TABLE IV.—SUCCESSIVE ANALYSIS OF SAMPLES OF ACETYLENE FROM THE SAME SOURCE BY THE VOLUMETRIC METHOD

Analysis No	Sample taken	Barometric pressure	Temperature	Acetylene found
1 ..	46.9	761.8	22.0	97.9
2..... .	45.5	761.8	22.0	98.0
3 . .	46.6	761.8	22.1	98.3
4 ...	44.8	765.4	22.1	98.1
			Mean =	98.1

The values given in Table IV show that with careful analysis very closely agreeing results may be obtained by the volumetric method, and that in the analysis of acetylene free from other absorbable hydrocarbons results are obtained which agree very closely with those given by absorption in fuming sulfuric acid.

When acetylene is prepared from ethylene dibromide by treatment with alcoholic potash there is always present a greater or less proportion of vinyl bromide, depending on the temperature and column of alkali through which the evolved gas is passed. In one sample collected this amounted to as much as 60% of the gas while the content of acetylene amounted to only 39%. Vinyl bromide undergoes rapid and complete absorption in fuming sulfuric acid and in neutral or ammoniacal silver nitrate. No distinction could therefore be made between acetylene and vinyl bromide by the Tucker and Moody method for determining acetylene. Vinyl bromide, however, does not give rise to any acidity in silver nitrate solution, and accurate results may therefore be obtained by the volumetric method in the analysis of acetylene mixtures containing this gas or any other hydrocarbon having a single or double bond.

Summary.

An account is given of a modification of the method of Chavastelon for the determination of acetylene in the presence of ethylene, or other single or double bond hydrocarbons, which is based on the volumetric determination of the nitric acid set free when acetylene is precipitated with excess of silver nitrate solution. When making an analysis according to this method, the sample is collected in an ordinary water-jacketed gas buret under observed conditions of temperature and pressure, and passed into an apparatus of simple design containing an excess of silver nitrate with which the gas is shaken until absorption is complete. Standard alkali solution is then added directly to the solution containing the precipitated silver acetylide until the brown color of silver oxide appears;

the excess of silver is then precipitated with neutral 20% sodium chloride solution, and the excess of free alkali in solution finally determined by titration with standard hydrochloric acid solution using methyl orange as indicator. Having calculated once for all the volume of acetylene under standard conditions of temperature and pressure to which 1 cc. of the standard alkali is equivalent, the acetylene in any sample analyzed follows directly from the volume of standard alkali required for the titration, and this volume of acetylene expressed in terms of the volume of the sample taken, when also reduced to standard conditions of temperature and pressure, gives the percentage of acetylene in the sample.

The method as described is rapid, accurate and simple of manipulation, and has the added advantage of giving accurate results for acetylene in mixtures of ethylene or of a gas of such similar properties as vinyl bromide which is readily absorbed in bromine, fuming sulfuric acid and in neutral or ammoniacal silver nitrate

EDGEWOOD, MD

NOTE.

The Use of Coal as a Substitute for Talcum to Induce Rapid Boiling.—While we were attempting to improve the method for the determination of small amounts of iodine, some substitute for talcum was sought which would cause a rapid boiling of the solution. The usual laboratory agents, such as pumice stone powdered brick, broken glass, glass beads, granite, etc., were tried and found to be unsuitable. The theoretically ideal agent would have to be insoluble in acid and alkali and not acted on by reduction or oxidation.

Carbon in its various forms answers the theoretical requirements. It was found, however, that the various forms of carbon differ greatly in their power to cause rapid boiling of a solution. While powdered charcoal or coke has slight power in this respect, anthracite coal is without exception the very best substance to bring about the rapid boiling of a solution. The formation of bubbles does not take place on the sharp edges and corners alone, but over the hard, smooth surfaces of the coal minute bubbles form with great rapidity, and under some conditions a piece of coal 2 cm. cube can be raised from the bottom of the flask by the rapid formation of bubbles on its surface. It acts in a similar manner in the acidification of a carbonate or sulfite solution. The bubbles of sulfur or carbon dioxide are liberated on the surface of the coal. Coal is equally successful in preventing bumping in Kjeldahl flasks and in the distillation of organic liquids. If the coal is kept under water indefinitely it becomes less active, but heating in an oven will restore its activity, Another great advantage of coal is the fact that it is easily cut with a dental drill and a small glass hook can be inserted in the coal. After the solution has been boiled, if it is so desired, the coal may be removed by a glass rod with a hooked end which passes through the glass hook in the coal. One or two pieces about 1 cm. cube are better than many smaller pieces. As powdered anthracite coal has almost no effect, the specific and unusual properties of hard coal in this regard must be due to its structure in the mass. E. C. KENDALL.

MAYO FOUNDATION,
ROCHESTER, MINN.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF FOREST PRODUCTS, UNIVERSITY OF WISCONSIN.]

ON THE QUINONE-PHENOLATE THEORY OF INDICATORS, ON THE REACTIONS OF PHENOLSULFONPHTHALEIN, AND ITS BROMO AND NITRO DERIVATIVES, AND THEIR MONOBASIC AND DIBASIC SALTS.[1]

BY E. C. WHITE AND S. F. ACREE.

Received July 27, 1918

The quinone-phenolate theory of indicators was brought out fully in 1908 by one[2] of the authors of this paper to explain the striking changes of color produced by the addition of alkalies to solutions of aurine, phenolphthalein and analogous substances. The chief color change was assumed to be merely the transformation of the faint yellow quinone-phenol, $—C(:C_6H_4:O)(C_6H_4OH)$, into the quinone-phenolate salt, $—C(:C_6H_4\cdot O)(C_6H_4OK)$, common to all these substances and absorbing the violet, blue, and green and transmitting the red light. The theory proposed was an attempt to correlate (1) the relations between the constitution and color changes of the rosaniline, aurine, and phenolphthalein salts on the one hand and (2) the mathematical relations of the tautomeric forms and the affinity constants and reaction velocities of the various acid and salt groups on the other hand, as had been done by the application of the mass law and conductivity and reaction velocity measurements to the urazole series.[3]

The work of Friedländer[4] and of Nietzki[5] and his students showed clearly that lactoidal colorless phenolphthalein (I) changes into salts of a colored quinoidal form (II),

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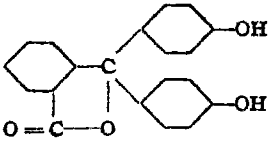
[1] The material presented in this paper and in two earlier articles (THIS JOURNAL, 39, 648 and 40, 1092 (1917)) represents a thesis presented to the Regents of the University of Wisconsin in 1915 by E. C. White, in partial fulfillment of the requirements for the degree of Doctor of Philosophy. The experimental work was performed partly in Johns Hopkins University, and partly in the Forest Products Laboratory, Madison, Wisconsin.

[2] *Am. Chem. J.*, 37, 72 (1907); 39, 155, 528 (1908).

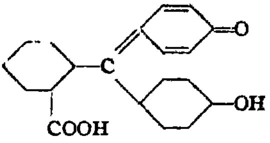
[3] *Ibid.*, 39, 124, 226 (1908)

[4] *Ber.*, 26, 172 (1893).

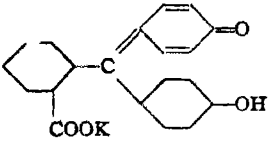
[5] *Ibid.*, 28, 45 (1895); 30, 175 (1897).



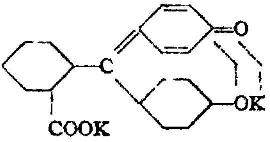
(I)



(II).



(III).



(IV).

and thus connected the constitution of these compounds with Ostwald's theory that indicators undergo changes of color because of simple changes in ionization without necessary attendant changes on chemical structure. Hantzsch,[1] and later Stieglitz,[2] developed this view mathematically and used Hantzsch's equation $C_Q \times C_H = K'' \times C_{I,H}$ for a tautomeric *monobasic acid.*

Our theory of indicators postulated that a simple change of the *dibasic* lactoidal phenolphthalein into the *monobasic* salt (III) is not sufficient to explain the remarkable colors produced and that the chief source of intense color is due to the presence of both a quinone group and the salt of a phenol (IV). In other words, we treated phenolphthalein as a dibasic acid giving dibasic red salts. Indeed it is hard to understand how anyone could have come to any other conclusion after having read Friedländer's paper showing the analogy between the color changes of aurine and phenolphthalein and their salts, which he assumed to be the *phenol salts* of quinones, $HOC_6H_4C(:C_6H_4:O)(:C_6H_4ONa)$ and $NaOOCC_6H_4—C(:C_6H_4:O)(C_6H_4ONa)$, or after having seen the significance of Nietzki's work showing that the *faint yellow* solutions of the quinoidal carboxyl ester of tetrabromo-phenolphthalein $(C_2H_5OOCC_6H_4)C(:C_6H_2Br_2:O)(C_6H_2Br_2OH)$, gave the *intensely blue* potassium and silver quinone-phenolate salts $(C_2H_5OOCC_6H_4)C(:C_6H_2Br_2:O)(C_6H_2Br_2OK)$. Notwithstanding these facts, there had been necessarily much confusion and lack of logic and vision in attacking these problems, and it must be realized that there is still great uncertainty concerning many of the dyes used today. Even with the above mentioned aurines, we realized that it was not certain whether the mono- or dibasic salts, or both, give the intense colors, and much interesting light has been shed on this by Paulus, Schaeffer and Jones. Even though we used as evidence for the theory the intense colors of the ester salts of phenolphthalein discussed above, and those described by Green,[1] yet we realized[2] that the intense color might arise from mono- and dibasic salts formed by saponification of the ester group. Meyer[3] and Spengler thought that they *proved* that the deeply colored salt of phenolphthalein is *dibasic* because they found that phenolphthalein dissolves as a *red solution* in approximately two molecules of alkali. The real lack of *proof* in such a case is seen at once when we recall that Slagle[4] and one of us found wide variations in the amount of alkali required to dissolve various indicators and derivatives, the results depending on the solubility and hydrolysis constants. Another example of the inconclusive nature of Meyer's evidence is shown by the fact that phenolsulfonphthalein dissolves in one molecule of dilute alkali as a *yellow monobasic* salt which, however, *looks red* if there is a slight excess of alkali as in Meyer's experiments: in such a case one would incorrectly draw Meyer's conclusion that the solution of the *mono* alkali salt of phenolsulfonphthalein is *red*, whereas it is really *yellow*. In other words a *red mono-* or other salt might have been mixed with the *apparent* dibasic salt which Meyer made, just as *dibasic* sodium sulfate can be colored with a small trace of dye. Baeyer developed his once widely accepted carbonium valence theory on the wrong idea that *p*-oxy-diphenylphthalide in alkaline solutions has a *red color*, which he afterwards found was really caused by a trace of phenolphthalein present as an impurity. Even with all this mass of evidence made uncertain by the possible presence of colored impurities in these compounds, and with the uncertainty whether there must be a *second* ion in combination with the quinone-phenolate salt and its ion, we thought that certainly the quinone-phenolate theory was worthy of investigation. What was most needed was the preparation of a series of *yellow monobasic salts*[5] and *red dibasic salts* of *pure* compounds of the phenolphthalein type, and these we have now made in the phenolsulfonphthalein series, and are studying extensively by the use of spectrophotometric methods and the hydrogen electrode.

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[1] *Ber.*, 39, 1090 (1906).

[2] THIS JOURNAL, 25, 1112 (1903). These ideas were abandoned after the appearance of our paper in 1908.

Not only was the quinone-phenolate group $—C(:C_6H_4:O)(C_6H_4\overset{-}{O}\overset{+}{K})$ thought to be deeply colored but it was pointed out that the intensely colored double compounds discovered by Jackson[6] when he mixed quinones and phenolate salts, for example, $O:C_6H_4:O.2C_6H_5ONa$, may also be present in solutions of the dibasic salt (IV) of phenolphthalein and analogous substances, a fundamental relation overlooked by those acquainted for years with Jackson's work. Whether the combination of the quinone with the phenolate ion or with the nonionized phenolate salt is chiefly responsible for the color change was left for future work.

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[1] *Ber.*, 40, 3724 (1907).

[2] THIS JOURNAL, 38, 2774 (1916).

[3] *Ber.*, 38, 1318 (1905).

[4] *Am. Chem. J.*, 42, 115 (1909).

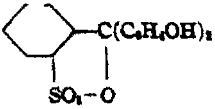
[5] Although the yellow carboxyl esters of phenolphthalein, $ROOCC_6H_4C(:C_6H_4:O)(C_6H_4OH)$, have been isolated, the corresponding yellow carboxylate salts have not been made. As these must be present in the incompletely neutralized solutions of phenolphthalein and its homologues we expect to measure the concentrations of such mono- and dibasic salts by the spectrophotometric methods which we are now employing.—BRIGHTMAN AND ACREE.

[6] *Am. Chem. J.*, 18, 1 (1894); 34, 441 (1905).

Equations were developed to show that the "apparent" affinity constants of the indicators involved the equilibrium constants of the different tautomeric forms, and the ionization constants of both the carboxyl group and the phenol group, as had already been proved experimentally with the urazoles. Contrary to the views of Hantzsch and Stieglitz, that a *large* affinity constant for the *carboxyl* group would cause a *greater* tendency to produce the red color or red salt, our equations showed that the addition of a small fraction of a mol. of alkali to a strongly acid carboxyl group would cause the formation of a *greater* amount of the faint yellow carboxyl salt and hence *less* of the (dibasic) phenol salt of such carboxyl salt and *less* intense color. At that time we had developed and applied to the urazoles the equations for only *monobasic tautomeric acids*, but we pointed the way[1] for the extension of these methods to dibasic acids when we could take up the quantitative study of this indicator theory. The equations covering fully the complete theory have now been developed by Birge and Acree and applied extensively in work soon to appear. This theory and our equations have meanwhile been accepted and developed further for special cases in the last few years by Wegscheider, A. A. Noyes, Rosenstein, Biddle, Willstaetter, Bjerrum, Jones, Schaeffer and Paulus, Lubs and Clark, and Cain.

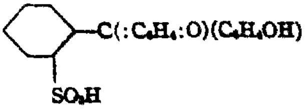
Theoretical Discussion of the Sulfonphthalein Series.

Owing to the necessity for preliminary work on the theory that both the ions and molecules of electrolytes are chemically active, which had to be completed before we could explain the reactions of alkyl halides with salts of indicators, the quantitative study of the quinone-phenolate theory of indicators was delayed until the investigations on the color changes produced by the addition of alkalies to phenolsulfonphthalein and its derivatives were taken up in 1914–15 in understanding with Professor Remsen,[2] who first developed this group in 1890.



Colorless lactoid.

(V).



Yellow quinoid acid.

(VI).

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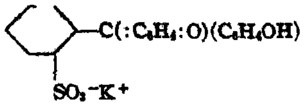
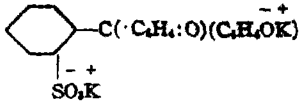
[1] Acree, *Am. Chem. J.*, 39, 528, 540, 542 (1908).

[2] *Ibid.*, 20, 257 (1898); 25, 201 (1901).



Yellow quinoid salt.
(VII).



Intense red quinone-phenolate salt.
(VIII)

The sulfonphthaleins were chosen for further work because it seemed probable that they would yield definite monobasic and dibasic salts and hence give final crucial evidence that the chief cause of the intense color in alkaline solutions is due to the dibasic quinone-phenolate salt (IV) and (VIII), and that the monobasic salt (III) and (VII) postulated formerly by others as a deeply colored salt, would prove to have only a faint yellow color arising from the quinone, in accordance with our theory. These salts were prepared about 4 years ago and since we have now completely substantiated the theory by spectrophotometric methods the work will now be described. The properties of the sulfonphthaleins are almost ideal for a study of this kind. In the first place they are soluble in both water and alcohol, like most sulfonic acids, and unlike the phenolphthaleins. In the second place, the substances are colored in the solid state and in solution and would seem to exist in part at least in the quinoidal condition (VI). This fact reminds us of the deep color shown by fluorescein and eosin, which show a decided contrast to phenolphthalein, which is *colorless in the solid state and in solution.* If the colored phenolsulfonphthalein exists appreciably in quinoidal form in solution, the fact should be demonstrated readily not only by the color changes but especially by the affinity constants of the sulfonic acid and of the phenol groups as determined by conductivity methods,[1] the hydrogen electrode, catalytic methods, and colorimetric or spectrophotometric[2] methods. A glance at the Formulas V and VI shows that in V we have two phenol groups which are certainly very weak acids. In Formula VI we have a sulfonic acid and a phenol within the same molecule. The sulfonic acids are very strong acids, approaching the mineral acids in affinity constants, and the direct measurement of the conductivities of the solutions of the phenolsulfonphthaleins and the use of the ionic velocities found for such substances should, therefore, give us some measure of the relative per cent of (V) and (VI). This is in decided contrast to the fact that the carboxyl groups of solutions of phenolphthalein, fluorescein, and eosin give so few ions and the conductivities are so small that this direct method can not be used. The conductivities of phenolsulfonphthalein at various concentrations have been used[3] as a direct measure of the per cent. of the quinoidal form in the solution and these results have been verified to some extent by corresponding measurements by the use of the hydrogen electrode, and spectrophotometric[1] data for the free acid and its mono- and dibasic salts. Since the lactoidal phenolsulfonphthalein is doubtless colorless, the yellow color given by the monobasic salt (VII) and that given by solutions of the free acid could also be used as a measure of the per cent. of the quinoidal form in equilibrium with the colorless lactoidal substance.

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[1] White and Acree, THIS JOURNAL, 39, 648 (1917).

[2] White and Acree, *Ibid.*, 40, 1092 (1918).

[3] White and Acree, *Loc. cit.*

The addition of alkalies to solutions of the sulfonphthaleins and the isolation of mono- and dibasic salts has allowed us to differentiate between the colors and spectra of the monobasic[2] salt (VII) and the dibasic salt (VIII) and has given evidence which has decided beyond question whether the monobasic salt or the dibasic salt is responsible for the intense color changes. A consideration of the affinity constants[3] of the sulfonic acids, about 10^{-1}, and of the phenols about 10^{-8} to 10^{-10}, makes it clear that the addition of an alkali to a solution of a mixture of the quinoidal and lactoidal phenolsulfonphthalein would result in the production of practically only the sulfonate salt in the first stages of the titration and that only toward the end of the introduction of one molecule of alkali would the partition of the alkali between the remaining free sulfonic acid and the entirely free phenol result in the production of appreciable quantities of the intensely colored dibasic salt. If the yellow color and spectrum of the solution of the phenolsulfonphthalein arise merely from the presence of the quinone group, uncombined with appreciable amounts of ionized or nonionized phenols, the monobasic salt (VII) should have practically only the same yellow color, which would change to an intense red only after the addition of sufficient quantities of alkali to neutralize a part of the phenol group in (VII) and allow the formation of the quinone-phenolate salt and the intensely colored double compound (IV) and (VIII) arising from the union of the quinoidal group with the phenolate ion or the nonionized phenolate salt. Since it requires 0.85–0.95 mol of alkali to change the yellow acid noticeably into a red salt, whose concentration increases until 2 or more mols of alkali are added, the evidence is fortunately so conclusive that there is no doubt that the monobasic salt (VII) is yellow like the free acid and is only faintly colored in comparison with the intensity of the color of the deep red dibasic salt (VIII); and the absorption spectra substantiate this evidence.

.The comparison of the colors of the *free* phenolsulfonphthalein with those given by the *free* tetrabromo and tetranitro derivatives gives us the much needed proof that the chief source of the intense color is a combination of the quinone with the phenolate *ion*. If the view were correct that the deep color of phenolphthalein comes from a monobasic carboxyl salt, it follows at once that a solution of phenolsulfonphthalein, with a high conductivity arising from the highly ionized sulfonic acid, should have a deep red color corresponding to the color of the red solution produced by the addition of two molecules of alkali. The facts are against this hypothesis, as the solution is yellow, because of the quinone group. If, on the other hand, the theory is correct that the solution becomes deeply colored only after the formation of *quinone-phenolate ions*, the addition of bromo or nitro groups to the phenol groups should (and does) increase the ionization and conductivity[1] of the phenol and hence causes the solutions of tetrabromo- and tetranitro-phenolsulfonphthalein to have much more of the corresponding blue and red colors given by the dibasic salts. Furthermore, the addition of hydrochloric acid to solutions of the free tetrabromo- and tetranitro-phenolsulfonphthalein should suppress the ionization of the phenol groups and hence change the intense blue and red colors to the faint yellow of the nonionized quinone phenols, which become ionized and deeply colored again when the acid is neutralized with alkalies or diluted with water. The bromophenol groups of the tetrabromo-phenolsulfonphthalein are not as highly ionized as are the nitrophenols and we find that the concentrated solutions show less of the blue. which comes out strongly on diluting the solution or adding alkalies, The nitrophenol groups, however, are much more highly ionized and give enough quinonephenolate ions to form an intensely red color which is very little accentuated by the addition of alkalies to deep layers of the solution studied. The addition of considerable hydrochloric acid suppresses the intense red to the yellow of the quinone-phenol. This yellow color changes into the red again when the solution is diluted with water or neutralized with alkali. Spectroscopic evidence favoring these views has already been published by us and the other descriptive matter is presented in this article.

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[1] White and Acree, *Loc. cit.* and data soon to be published by Guy, Birge, Brightman, Hopfield, Meacham and Acree.

[2] White and Acree, *Science*, 42, 101 (1915); THIS JOURNAL, 40, 1092 (1918).

[3] Lubs and Acree, THIS JOURNAL, 38, 2772 (1916).

The sulfonphthaleins are particularly adapted to this study for another reason. Although there is much left to be desired concerning the solubility of these substances, which we shall try to increase by the introduction of more sulfonic acid groups,[2] they are much more soluble in water and in alcohols than are the phenolphthaleins, fluoresceins, aurines, and analogous substances. It is easy to prepare 0.001 *N* solutions of phenolsulfonphthalein and of its tetrabromo and tetranitro derivatives, and

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[1] This Journal, 39, 648 (1917).

[2] This method of increasing the solubility of dyes and indicators by introducing sulfonic acid groups has been emphasized in lectures on dyes for a number of years and will be used as widely as possible, especially in the aurine and phenolphthalein series which are sparingly soluble in water.

Lubs has found thymolsulfonphthalein and its dibromo derivative to be even more soluble. It is, therefore, much easier to measure the colors and affinity constants of the sulfonphthaleins directly than can be done with the phenolphthaleins and this fact makes it much easier to study the changes in color and in affinity constants produced by substituent groups in the benzene sulfonic acid grouping and in the phenol groups. It is possible to introduce negative chloro, bromo and nitro groups, or basic amino or substituted amino groups, or neutral alkyl groups, or acid phenol and sulfonic acid groups, into both the benzene sulfonic acid and the phenol groups of the sulfonphthaleins and obtain a large number of homologues and derivatives of these substances having a wide range of "effective" affinity constants and useful hydrogen ion concentration ranges. This part of the synthetic work is now being prosecuted as rapidly as possible by us[1] and also by Professor Orndorff, who has reached an understanding with us and has begun work along similar lines involving the sulfonphthaleins. The measurement of the "effective" affinity constants of the sulfonphthaleins by both the hydrogen electrode and by very accurate spectrophotometric methods involving studies of "salt effects" was proposed by one of us and extensive investigations, partly completed, are under way.

Experimental.

Preparation of the Acid Ammonium Salt of Orthosulfobenzoic Acid.—This substance, which is the starting point in the preparation of phenolsulfonphthalein, is prepared by the hydrolysis of saccharine. 400 g. of saccharine is suspended in 6 or 7 liters of water to which 500 cc. of conc. hydrochloric acid has been added. The mixture is boiled until all the saccharine has been dissolved, and water is added to replace that lost by evaporation. The commercial saccharine available at present is very pure (ours was obtained from the Monsanto Chemical Works, of St. Louis) and does not deposit the *p*-sulfaminebenzoic acid present as impurity in the material used by Remsen and his students. After solution of the saccharine the liquid is evaporated to about 600 cc., with constant stirring when the volume becomes small. On cooling, most of the acid ammonium salt crystallizes out.

Preparation of the Anhydride of O-sulfobenzoic Acid.—This substance has been variously prepared—by heating the acid, by distilling the acid with phosphorus pentoxide, and by the action of chlorinating agents on the acid salts. The first method is unsatisfactory, for the acid loses its water with great difficulty. The second method also is unsatisfactory, because of the bulk of the pentoxide needed when any considerable quantity of the anhydride is to be prepared, and also because the dehydration is accompanied by excessive charring. The distillate of the anhydride, moreover, is likely to be dark colored, owing to volatile impurities carried over with it. Both these methods are also open to the objection that the free acid is hard to prepare.

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[1] See Davis and White, *J. Urology*, 2, 107 (1918), for the synthesis of a number of important compounds in the sulfonphthalein, phenolphthalein and other series.

The most satisfactory method for the preparation of the anhydride involves the use of thionyl chloride. After we had developed the use of this reagent, which we have applied extensively, we learned that Cobb[1] had used this reagent on the acid potassium salt, and obtained a yield of 80% of the anhydride. The action of the thionyl chloride seems to be confined entirely to the carboxyl group. We have modified this method somewhat, and have obtained nearly theoretical yields, even though the method involves the extraction of the anhydride by means of benzene. We used the acid ammonium salt instead of the potassium salt, and found it unnecessary to use the large amounts of thionyl chloride recommended by Cobb. Enough of the chloride is used just to wet the salt thoroughly. The salt must be finely powdered. The mixture, under a reflux condenser, is heated on the water bath for 3 hours; the excess of the chloride is distilled off *in vacuo*, a small amount of the anhydride being carried along. The residue, consisting of the anhydride and ammonium chloride, forms a hard cake, and the flask must sometimes be broken in order to remove it. It is broken up and extracted with dry benzene. The use of the usual paper thimble is not permissible, as the paper chars badly and contaminates the product. The benzene solution darkens somewhat as the extraction proceeds, but on cooling it deposits beautiful, colorless crystals of the anhydride. Typical preparations gave the following yields:

1 50 g. acid salt and 80 g thionyl chloride gave 30 g. anhydride, corresponding to a yield of 80%.

2 150 g acid salt and 200 g. thionyl chloride were used. 60 g. of the chloride was recovered. 115 g of the anhydride was obtained, or 91% of the theory.

Preparation of Phenolsulfonphthalein.—As the product of the action of thionyl chloride on the acid ammonium salt should consist of only ammonium chloride and the anhydride, there appeared to be no reason why we should not proceed directly to the preparation of phenolsulfonphthalein by heating such a mixture with phenol, without previously extracting the anhydride. We made many attempts to prepare the anhydride in this way, but were unsuccessful. The mixture, when heated for 24 hours at 130–135°, formed a red, tarry mass, which on boiling with water became oily. The oil dissolved in alcohol to give an orange solution, from which crystals, presumably of benzoic acid, separated. They were recrystallized several times by dissolving in alcohol and reprecipitating with water, and then showed the melting point of benzoic acid. This was not changed by mixing the substance with benzoic acid. We made no further attempts to identify the other substances.

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[1] *Am. Chem. J.*, **35**, 502 (1906).

By heating the pure anhydride with phenol, formation of the phthalein readily takes place.[1] 108 g. of the anhydride was mixed with 120 g. of phenol, and heated in an oil bath at 130–135°. The mixture fuses to a yellow liquid as soon as the phenol melts. The color soon becomes deep red, and the liquid slowly becomes opaque and viscous. The maximum viscosity seemed to be reached after about 6 hours' heating; 18 hours further heating produced no appreciable difference. The product displayed a green-red irridescence. The excess of phenol was distilled out with steam, the residue washed with water, dissolved in alkali, filtered from a small amount of insoluble matter, and precipitated with acid. It was then washed again and dried.

We made many attempts to find a means of crystallizing this material. It is only slightly soluble in all the solvents that were tried, with the exception of hot phenol and glacial acetic acid. One g. of the material was dissolved in about 50 cc. of boiling phenol. The solution was allowed to cool as far as possible without solidification, and a large amount of ether was added. A very fine, granular powder separated out, which under the microscope showed poorly crystalline form. This powder was thoroughly washed with ether to remove phenol and dried at 120°. It is more soluble in water than the product obtained by precipitation from alkaline solution, and is lighter in color. The difference in solubility is doubtless due to the smaller size of the particles.

Titrations of Phenolsulfonphthalein.[2]—The powder is soluble in water to the extent of 0.03 g. in 100 cc. Solution is extremely slow, and the water must be boiled vigorously. The solution sometimes shows a slight cloudiness, but the amount of material in suspension from 0.03 g. of the phthalein is not weighable.

The alkali used in the titrations was prepared by dissolving sodium in freshly boiled distilled water. The solution was titrated against hydrochloric acid that had been standardized gravimetrically, and was used immediately against the phthalein solution.

From what has been said in the earlier part of this paper, we should expect that when alkali is added to such a phthalein solution the first reaction would be the formation of a monobasic salt, a sulfonate. This reaction should continue until approximately all of the sulfonic acid is neutralized, when the alkali should act on the phenolic hydroxyl and thus form an intensely colored dibasic salt. According to the quinone-phenolate theory, the solution of the monobasic sulfonate should not differ materially in color from that of the free acid; hence, we should be able to add to the solution of the acid approximately one equivalent of alkali without the appearance of a color change, but on further addition of alkali an intense color should appear, due to the formation of the dibasic salt, which contains the quinone-phenolate complex, whereas the free acid and the monobasic salt do not.

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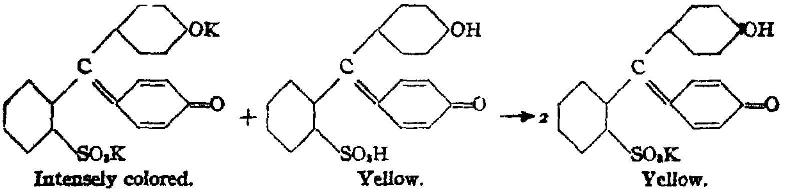
[1] At the suggestion of one of us Mr. L. R. Baldwin has shown that stannic chloride is an excellent condensing agent for the preparation of phenolphthalein from phthalic anhydride and phenol. We expect to use the stannic chloride, and other similar salts easily decomposed by water, widely in the preparation of phthaleins, sulfonphthaleins and similar compounds.

[2] The material used in some of these titrations was kindly furnished by Mr. H. A. B. Dunning of the firm of Hynson, Westcott & Dunning, Baltimore.

A saturated solution of phenolsulfonphthalein in water has an orange color. This is what we might expect from the fact that the dye has a quinone group. If a drop of very dilute alkali is added, an intensely red or purple streamer appears locally, but disappears when the solution is stirred. As more alkali is added the phenomenon is repeated, until at a certain point the solution develops a red tinge which does not disappear on stirring. Two drops of 0.02 *N* alkali, or about 0.10 cc., make this color change marked.

Although we have carefully considered the possibility that some of these color phenomena may arise from impurities in the phenolsulfonphthalein, we believe that the explanation of these color changes is obvious. When a drop of alkali is added to the orange solution, the alkali is *locally* in excess of the phthalein, and some of the intensely colored dibasic salt is formed. As this is stirred up, it is acted upon by the free acid, with the formation of the monobasic salt, which is *not* intensely colored:—



The final appearance of the persistent red color is due to the permanent formation of dibasic salt.

The following data show the amount of alkali required to produce the permanent color change. Approximately 0.02 *N* alkali was found to be suitable for the titrations. In the column headed "cc. NaOH, theory" are given the number of cc. of alkali corresponding to one molecular equivalent with respect to the phthalein.

Titrations 1–6, inclusive, were made with material obtained from Hynson, Westcott and Dunning, the others were made with material of our own preparation, 10, 11 and 12 having been crystallized from phenol by the method already described. (Most recent preparations have required 0.93 to 0.95 mol alkali and further purification will be attempted for the very exact spectrophotometric data.—S. F. A.)

No.	Wt. of phthalein	Vol. of solution. Cc	Cc. NaOH, theory.	Cc. NaOH found.	% of 1 mol. eq.
1	0.0314	300	4.28	3.75	87.6
2	0.0310	150	4.28	3.73	87.1
3	0.0288	125	3.99	3.43	87.2
4	0.0322	200	4.40	3.77	85.6
5	0.0176	20	2.40	2.10	87.5
6	0.0420	150	5.73	4.97	86.6
7	0.0131	100	1.73	1.51	87.2
8	0.0389	300	5.95[1]	4.76	80.0
9	0.0329	300	5.03	3.96	78.7
10	0.0297	...	4.54	4.11	90.5
11	0.0252	...	3.86	3.49	90.4
12	0.0329	...	5.04	4.41	87.5
					Av., 86.3

The fact that less than one equivalent of alkali is required is explained as follows: as more and more of the sulfonic acid is neutralized, the ionization of the remaining sulfonic acid is suppressed, and its acidity is, in effect, lowered. When approximately 95% of one molecular equivalent of alkali has been added, there are present about 100 parts of phenol hydroxyl to every 5 parts (*at most*, depending on the purity) of sulfonic acid still unneutralized. Since the ionization of this remaining free sulfonic acid is reduced by the presence of the sulfonic acid salt already formed, the phenol can at this point visibly compete with the sulfonic acid for the alkali. Hence, further addition of alkali results in the formation of the phenolate group, with the consequent appearance of intense color. These figures vary, of course, with the purity of the compound and the substituent groups, as has been shown by Lubs and Acree.[2]

These titrations show, then, that we can add nearly one molecular equivalent of alkali before the appearance of a color change; in other words, the monobasic salt does not differ in color to any appreciable extent from the free acid.

Monopotassium Salt.—We have, moreover, *isolated* monobasic salts of phenolsulfonphthalein, although we are not sure that they are perfectly pure. In every case the color of the *solutions* of these salts is *orange;* the addition of alkali to these solutions produces an *intense purple color*, due to the formation of the dibasic salt. When solid phenolsulfonphthalein is stirred up with enough strong potassium hydroxide to dissolve it, the intense purple color is developed, but if an excess of the phthalein is now added, the solution, on stirring, becomes orange-red, and more of the phthalein dissolves. Such a solution, in which no more phthalein would dissolve, was filtered, and the rather viscous filtrate was evaporated to dryness on the water bath. The loss of water was slow, especially towards the end of the process. A glassy, brittle, dark-red residue was obtained. The material, after being finely ground in an agate mortar, was dried to constant weight at 120°. It was analyzed for potassium by converting it to potassium sulfate. As the digestion with conc. sulfuric acid was extremely difficult, the material was first ignited in a platinum crucible until the ash was perfectly white; this was dissolved in dil. sulfuric acid, carefully evaporated to dryness, and again ignited. It was found that the ash formed by the first ignition gained practically no weight by the treatment with sulfuric acid; hence it must have consisted almost entirely of sulfate.

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[1] A new standard alkali solution was used in this and succeeding titrations, which accounts for the fact that 8 required a larger *volume* of alkali than did 6, although Sample 8 was smaller than Sample 6.

[2] Lubs and Acree, This Journal, 38, 2772 (1916).

Potassium salt, 0.1510, 0.3877. K_2SO_4, 0.0327, 0.0821

Calc. for $C_{19}H_{13}O_5SK$. K, 9.98 Found 9.71, 9.50

Although the potassium content is a little low for the monobasic salt, there is probably a trace of the dibasic salt present also, for the color of the solution of the substance, while distinctly orange, is noticeably deeper than that of the free acid or of a solution of the free acid to which as much as 75% of one molecular equivalent of alkali has been added. When we consider how intensely colored the dibasic salt is, we see that a very small amount of it would affect the color of the monobasic salt very considerably. However that may be, the color of the product is so far different from that produced when more alkali is added to it that there can be no doubt as to the wide difference between the colors of the monobasic and dibasic salts.

In accounting for the low potassium content, we must consider that phenolsulfonphthalein is somewhat soluble in water, and the method of preparation of our monobasic salt permits the solution of a certain quantity. This lowers the potassium content of the product. The substance is, then, most likely contaminated with small amounts of dibasic salt and of free acid. The coexistence of the latter two would not be surprising, for we have the same condition when there has been added 86 to 95% of one equivalent of alkali in the titrations already described.

The monobasic salt is readily soluble in water and in alcohol, but insoluble in ether. If ether is added to the alcoholic solution an emulsion is formed, and on standing the salt forms a sticky mass on the sides of the vessel, and does not crystallize.

Mono-silver Salt.—When a water suspension of silver oxide and phenolsulfonphthalein is shaken up a purple color develops at first. If an excess of silver oxide is present, the purple color (dibasic salt) remains for a time, but soon a brown sludge forms, which is so finely divided that it passes through filter paper. This is probably due to the reducing effect of the phenol group upon the oxide. If, on the other hand, an excess of the phthalein is used, the purple color gives way to an orange one, and all the silver oxide dissolves. The solution, when filtered and evaporated in the same manner as the potassium salt, gives a material identical in appearance with that salt, and showing the same solubility and color of solution. On ignition it gives metallic silver, although we might expect that silver sulfide or sulfate would be formed from a silver salt of a sulfonic acid. The analyses follow:

Subs., 0.2556, 0.4153. Ag, 0.0591, 0.0958.

Calc. for $C_{19}H_{13}O_5SAg$: Ag, 23.39. Found: 23.12, 23.06.

Mono-calcium Salt.—Calcium carbonate in excess was shaken up with a water suspension of phenolsulfonphthalein and allowed to stand, with frequent shaking, for several days. The orange-colored solution was filtered and evaporated as in the other cases. A sample dried to constant weight was ignited, evaporated with sulfuric acid, and ignited again.

Subs., 0.1085; $CaSO_4$, 0.0210.

Calc. for $(C_{19}H_{13}O_5S)_2Ca$: Ca, 5.6. Found: 5.3.

This salt was similar to the other monobasic salts in every respect.

Pyridine Salt.—Phenolsulfonphthalein readily dissolves in pyridine. An excess of the latter was used, the solution was filtered and evaporated on the water bath. (The use of an excess of the dye gives a viscous mass from which the excess cannot be filtered.) The salt formed a soft, tarry mass, whose solution resembled in color that of the other salts. When heated to 110–120° it became hard and dry, but still smelt of pyridine. This odor did not disappear even when the salt was allowed to stand over sulfuric acid in a vacuum, and the attempt to remove the free pyridine by heating the material at 120° for a long time resulted in decomposition.

An attempt was made to prepare a pyridine salt by allowing the phenolsulfonphthalein to stand over pyridine in a desiccator. The substance attracted much pyridine, finally forming a liquid mass like that obtained in the previous experiment.

Ammonium Salts of Phenolsulfonphthalein.—These salts were prepared by the action of dry ammonia gas upon weighed quantities of the sulfonphthalein. The ammonia was generated by placing a mixture of lime and ammonium chloride in a desiccator, which also contained over this mixture a dish holding a large amount of sodium wire. The sulfonphthalein changed from a red to an almost black color very soon after it was placed in the atmosphere of ammonia, and this dark material dissolved in water with the intense purple color characteristic of the *dibasic* salt. When the dark material was allowed to stand in the air or over sulfuric acid, it gave off ammonia and slowly changed color back to the red of the original phthalein. This red material was evidently the mono-ammonium salt, for it was readily soluble in water, giving an *orange* solution, and on analysis gave the proper per cent. of nitrogen.

These changes are readily explained. When the phthalein is in the presence of excess of ammonia, a *dibasic* salt is formed, which is intensely colored and gives intensely colored solutions. It contains an ammonium *sulfonate* group and also a ammonium *phenolate* group. We should expect the former to be very stable, and the latter to be stable only in the presence of ammonia. Indeed, we might predict that the extent to which the ammonium phenolate would break up into the free ammonia and the phenol residue would depend upon the temperature and the pressure of the ammonia in the atmosphere in which the salt was placed. If it was placed over sulfuric acid, the ammonia given off would be continuously absorbed by the acid, and all of the ammonium phenolate would finally be decomposed. A monobasic ammonium sulfonate should be left, and according to the quinone-phenolate theory it should and does dissolve in water with approximately the same color as the free phthalein.

The quantitative results obtained show clearly that the dark material is the dibasic salt, and that the red material formed again when the dibasic salt is placed over sulfuric acid is the monobasic salt. Weighed samples of the phthalein were placed over the ammonia mixture and allowed to stay there until the maximum gain in weight was reached. Standing overnight was sufficient. It was found that the samples lost in weight slightly after this period; this loss is not surprising in view of what was said above in regard to the equilibrium conditions existing between the ammonium phenolate and its decomposition products. After the maximum weight had been thus attained, the sample was transferred to a sulfuric acid desiccator and allowed to stay there until minimum weight was attained. All weighings were made by quickly transferring the material to a tightly closed weighing glass, as the salts are very hygroscopic. Minimum weight was reached after standing over sulfuric acid for about two weeks.

Subs., (phenolsulfonphthalein) 0 1962, 0.2814. Gain, NH_4, 0 0190, 0.0270.
Calc. for $C_{19}H_{12}O_5S(NH_4)_2$: Gain, 9 60. Found· 9.68, 9.59.

After standing over sulfuric acid these gains were reduced to (I) 0.0100 g. or 5.09%; (II) 0.0137 g. or 4.86%. Monobasic NH_4 salt requires 4.80%.

In order to study the effect of substituent groups on phenolate formation, and consequently on color, we have prepared bromination and nitration products of phenolsulfonphthalein. The bromine and nitro groups are strongly negative, and their introduction into the phenol residue in ortho position with reference to the hydroxyl increases the acidity of the phenol. We should therefore expect a more ready formation of intense color than in the case of phenolsulfonphthalein.

Tetrabromo-phenolsulfonphthalein.—Remsen and Sohon[1] obtained a dibromo substitution product by the action of bromine on phenolsulfonphthalein, and were unable to obtain a tetrabromo derivative even when sufficient bromine was present. The experiments of Remsen and his students with other sulfonphthaleins also led to the preparation of compounds with only two substituted bromine atoms. We have, however, obtained a well defined tetrabromo substitution product. Evidently the experimental conditions used in the excellent work of Remsen and Sohon differed from ours in an unknown way.

In one experiment 7 g. of sulfonphthalein, 5 cc. of bromine and 150 cc. of acetic acid were used. The solid material did not dissolve even on long standing, but changed over to an orange-colored, well crystallized material. When filtered off, this appeared pinkish It was subjected to further treatment with bromine under the same conditions as before, and the appearance did not change. The acetic acid—bromine solution from the yellow material was evaporated on the water bath. A dark red, tarry mass was formed. For this reason it is not advisable to use a large amount of acetic acid in the preparation of the tetrabromo derivative; the material contained in solution crystallizes out only very slowly, and attempts to obtain it by concentration invariably result in decomposition.

A much more satisfactory method is the following: Five g. of phenolsulfonphthalein is suspended in 40 cc. of glacial acetic acid. The acid is heated almost to boiling and there is added little by little a solution of 5 cc. of bromine in 20 cc. of glacial acetic acid, while keeping the original mixture just below the boiling point. Evolution of hydrobromic acid begins as soon as the first of the bromine is added. The phenolsulfonphthalein gradually dissolves, and in its place a crystalline precipitate of the tetrabromo derivative settles out. Yield 7.5 g. These crystals are almost colorless, but when they are filtered they acquire a pink color as soon as the acetic acid is drained from them. This color changes to orange, but is removed if the crystals are again moistened with the acid, returning again when the material is drained. This phenomenon does not appear to be one of oxidation and removal of the oxidation product by acetic acid, for it appears when the wet crystals are dried in a current of carbon dioxide. After a time the dry crystals assume a flesh color, which seems to be uniform and which has not changed after keeping for more than two years.

The product thus prepared, and washed free of bromine with acetic acid, is pure, giving the following analysis after drying in the air:

Subs., 0 1464; AgBr, 0.1628.
Calc. for $C_{19}H_{10}O_5SBr_4$: Br, 47.7. Found: 47.3.

The material can be recrystallized from boiling glacial acetic acid, but a large amount of acid is required and solution is slow. A more satisfactory solvent consists of a mixture of acetic acid and acetone, in the latter of which the substance is very soluble. The recrystallized substance showed the same bromine content as did the first crystals.

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[1] *Loc. cit.*

Subs., 0.1902; AgBr, 0.2115.

Calc. for $C_{19}H_{10}O_5SBr_4$· Br, 47 7. Found. 47.3.

The behavior of this substance when heated in the capillary tube is characteristic. At about 210° a greenish sublimate appears, and the substance becomes a deeper orange in color This then melts sharply at 270–271°, with decomposition and gas evolution. We intend to investigate this substance further.

Di-ammonium Salt of Tetrabromo-phenolsulfonphthalein.—This salt was prepared in the same manner as was the mono-ammonium salt of phenolsulfonphthalein. It was found that tetrabromo-phenolsulfonphthalein absorbed an amount of ammonia much in excess of that required for a dibasic salt; the product formed by the absorption was allowed to stand over sulfuric acid until minimum weight was reached. The gain indicated a stable *dibasic* salt. This is what we might expect, for the bromophenol is a stronger acid than the phenol of phenolsulfonphthalein, and can therefore hold the ammonia more firmly.

Subs , 0.2472, 0 2526. Gain, NH_3, 0 0141, 0 0126

Calc. for $C_{19}H_8O_5SBr_4(NH_4)_2$ Gain, 5 1 Found 5.7, 4 9.

Preparation of Tetranitro-phenolsulfonphthalein.—Five g. of phenolsulfonphthalein is dissolved in 30 cc of cold conc. sulfuric acid. Solution is slow, and must be aided by shaking. A dark red solution results. Conc. nitric acid is added a little at a time until the precipitate first formed no longer dissolves on agitating the mixture. The solution is then poured into a moderate amount of water (about 100 cc.). A voluminous, bright yellow precipitate separates out. Where the solid is in contact with water a red color appears, but as the red portion is stirred up and comes in contact with acid it becomes yellow. The pasty precipitate is filtered on the pump; if allowed to stand long before filtration it goes over to a colloidal form, and this material cannot be filtered. The precipitate is washed with water. Complete drying by suction is impossible, as the water is held tenaciously. The material is purified by crystallization from boiling acetic acid, or better from a mixture of acetic acid and acetone. The crystals are minute, glistening flakes, which when dry have a canary yellow color.

The substance showed no sharp melting point, slowly passing to a shellac-like material above 200°. It was analyzed for nitrogen by the Kjeldahl method, thiosulfate being used as a reducing agent.

Subs., 0.2653, 0.2494. Cc. 0.0714 *N* H_2SO_4, 26.7, 27.5.

Calc. for $C_{19}H_{10}O_5S(NO_2)_4$· N, 10.5. Found: 10.0, 11.0.

[illegible] onium Salt of Tetranitro-phenolsulfonphthalein.—This salt [illegible] red in the same manner as the other ammonium salts already [illegible] Here again the substituted phenol is a sufficiently strong acid [illegible] monia firmly, and a dibasic salt is therefore formed.

[illegible] ubs., 0.2407, 0.1869. Gain, NH_3, 0.0158, 0.0127.

[illegible] alc. for $C_{19}H_8O_5S(NO_2)_4(NH_4)_2$: Gain, 6.3. Found: 6.5, 6.7.

[illegible] or Changes of Tetrabromo-phenolsulfonphthalein and of [illegible] -phenolsulfonphthalein, and their Interpretation.—(*a*) Tetra- [illegible] nolsulfonphthalein is soluble in water to the extent of at least [illegible] liter. A solution of this concentration has a dark, dirty red [illegible] *is changes to an intense blue when alkali is added to the solution,* [illegible] *e solution is diluted.* If alkali is added to a *very dilute* solution [illegible] omo-phenolsulfonphthalein, already deep blue, *no noticeable* [illegible] *color takes place.*

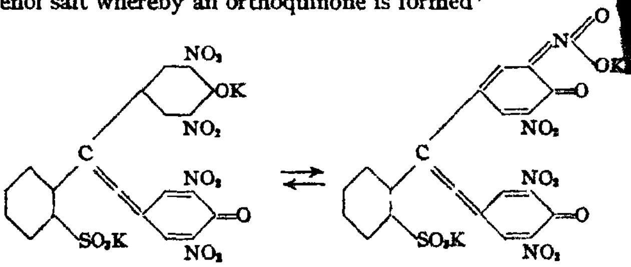
The [illegible] ition of any strong acid to a blue solution of tetrabromo-phenol- [illegible] lfon [illegible] alein causes a gradual change of the color through various [illegible] ighter [illegible] des, and the solution finally becomes deep yellow.

The [illegible] color phenomena can all be explained on the assumption that it [illegible] *one-phenolate ion* (or the complex that the phenolate ion forms [illegible] quinone group) that is the cause of intense color. The substitu- [illegible] omine atoms in ortho position to the phenol hydroxyl of phenol- [illegible] thalein increases the acidity of the phenol; hence there is an [illegible] ble formation of phenolate ions in a water solution of the tetra- [illegible] ompound, whereas the phenol of the unbrominated compound is [illegible] k an acid that it gives no appreciable quantity of phenolate ions, [illegible] the solution is *not* intensely colored, but becomes so only on the addi- [illegible] of alkali. The extent of the ionization of the bromophenol would be increased by dilution of the solution or by the addition of alkali, hence either of these processes intensifies the color of the solution.

The addition of acid to a blue solution of tetrabromosulfon- [illegible] halein *gradually* changes the color to yellow because the ionization of [illegible] phenol is suppressed more and more as the hydrogen ion concentration increases.

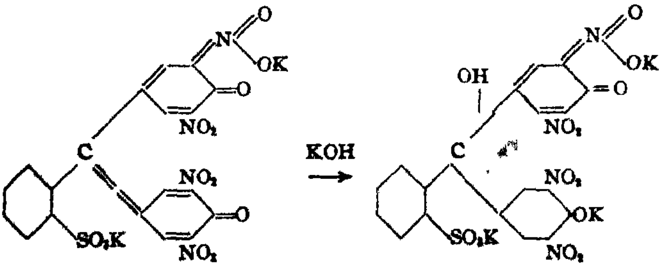
(*b*) Tetranitro-phenolsulfonphthalein, a yellow powder, dissolves in water (or alcohol) with the production of a beautiful purple-red solution. The color resembles that of a solution of phenolsulfonphthalein to which two molecular equivalents of alkali have been added. Evaporation of the solution of the tetranitro compound gives back the yellow powder. If two equivalents of alkali are added to the solution, *absolutely no visible change in color takes place in deep layers. The solution shows precisely the same absorption band before and after the addition of alkali in a 30 cm. tube.* As these deep layers of the acid give enough quinone-phenolate ions to absorb the green light, thin layers will be used in the spectrophotometric work. A solution of the *tetrabromo* compound of normality *does* show a change in color when alkali is added. T because a solution of the bromo compound contains a considerab of *undissociated* phenol and much less of *phenolate ions*, and violet and green is not all absorbed; the addition of the alkali further conversion of the phenol molecules into these ions, and hen absorption. The dinitrophenol group of the tetranitro-phe phthalein is a much stronger acid than the corresponding dibro and is therefore more fully dissociated in solution. It therefo the addition of much more acid to the tetranitro than to the te derivative to suppress the ionization of the phenols and change color back to yellow. Consequently, the addition of alkali to a the nitro compound does not so greatly increase the concentra phenolate ions, and there is therefore no appreciable increase in th of the color in the deep layers which already absorb practically all

If a considerable amount of alkali is added to the solution of compound the color changes from purple-red to yellow. Ad acid brings back the intense purple-red color. It seems likely fading may be connected with two processes: (1) a rearrangeme nitrophenol salt whereby an orthoquinone is formed:



Intense red. Yellow

and (2) with a hydration effect whereby the paraquinone is destro with the formation of a tribasic salt:[1]



Yellow.

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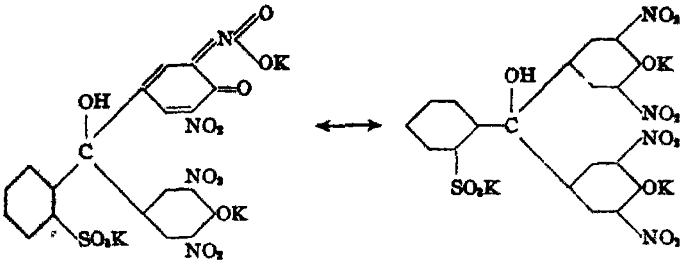
[1] Cf. Green and Perkin, *J. Chem. Soc.*, 85, 398 (1904); Kober and Marshall, This Journal, 33, 1779 (1911).



Yellow(?). Colorless

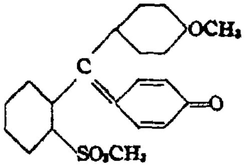
The second nitrophenolate thus formed might rearrange into a second orthoquinone, and the yellow color of the solution could then be accounted for by the presence of two orthoquinones, which are not intensely colored. It is obvious that the bleaching by alkalies may be a very complicated process, and that the addition of acid to the solution simply reverses these reactions.

When a drop or two of strong hydrochloric acid is added to a solution of the free tetranitro compound no appreciable color change takes place. As more acid is added the color fades to yellow. *Addition of water to the yellow solution brings back the purple-red* color. The hydrochloric acid suppresses the ionization of the nitrophenol, hence the color fades The ions and the color return when the solution is diluted.

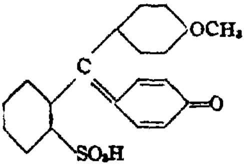
Action of Diazomethane on Phenolsulfonphthalein.—The phenolsulfonphthalein was suspended in ether and treated with diazomethane until the powder had become yellow and no longer gave any trace of color with alkali Only a small part of the yellow material was found to be in solution. This slowly separated out in the form of minute crystals, which melted sharply at 158°. Further evaporation of the solution did not give more of the crystalline material; a dark red, tarry substance was left when the mother liquid was evaporated to dryness. The crystals did not change their melting point when they were recrystallized from carbon tetrachloride, so they were assumed to be pure. The bulk of the yellow powder, which had not dissolved in the ether, showed a melting point of of 150–154°. Recrystallization gave a product which melted sharply at 158°. The mother liquor from this substance usually deposited nothing until it had been evaporated to complete dryness, when the dark red material mentioned above was left. Attempts to crystallize this red material failed.

The substance which melts at 158° is insoluble in cold water and in cold alkali solution, even though it be very concentrated. When boiled with water it slowly dissolved, giving a deep yellow or orange solution, which gave no color on addition of alkali. On boiling some of the substance with alkali it dissolved very slowly, and the solution developed a pale red tinge. The substance dissolved readily in conc. hydrochloric acid with a deep red color. Green and King[1] prepared an ester-hydrochloride of phenolphthalein which was deep red, whereas the ester itself was yellow.

The color of the substance indicates that it is a *quinoid* ester. Its insolubility in cold alkali solutions shows that it cannot be a mono-ester, for such an ester would have one free acidic group and would be soluble in alkali. It is to be assumed for the present that it is a quinoid di-ester of the constitution



and further work now in progress will throw more light on its structure. Such an ester would be the normal product of the action of diazomethane on quinoidal phenolsulfonphthalein. It would be expected that the sulfonic ester would be very readily saponified by alkali and hydrolyzed by water, and that the resulting mono-ester



would be soluble in alkali with approximately the same color as a solution of free phenolsulfonphthalein. The fact is, however, that the di-ester must be boiled with water or alkali to effect solution.

The attempt to determine the amount of sulfur in this compound by Carius' method failed. A colorless, crystalline substance was formed in the tube, and it was not decomposed even after heating for 4 days at 250–300°. The limited amount of the material at our disposal made other analyses impossible.

Action of Diazomethane on Tetrabromo-phenolsulfonphthalein.—The bromine derivative was treated with diazomethane until it no longer gave any trace of blue color with alkali. A bright yellow powder was formed. By recrystallization from benzene a product was obtained which seemed to become semi-fluid between 155 and 160°. This then solidified, a contraction being noted, and the new material, which had a slightly deeper color, melted at 232–234°. Further crystallization from benzene eliminated the change at 155–160°, and the material then melted sharply at

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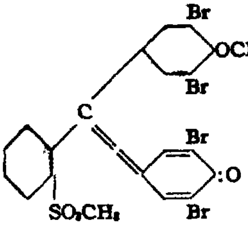
[1] *Loc. cit.*

234–235°. This point was not changed by further crystallization. The pure product was similar to the crude product in solubility and behavior towards alkali. It was insoluble in water and alkali, and even vigorous boiling did not affect the material in any way. It was soluble in alcohol and in acetic acid, very slightly soluble in ether. It is possibly a quinoid ester of the structure



and we are now investigating the constitution further. It seems strange, however, that a sulfonic ester should be stable in the presence of boiling solutions of alkali.

Conclusions.

1. Methods have been described for the preparation of phenolsulfonphthalein, tetrabromo-phenolsulfonphthalein, and tetranitro-phenolsulfonphthalein, and their properties and color changes have been described.

2. Although monobasic carboxylate yellow salts of phenolphthalein have not been isolated, the corresponding monobasic yellow salts of the phenolsulfonphthalein series have been made and described by us and later by Lubs and one of us. These salts have been studied spectrophotometrically and shown to resemble the free acids very closely. They cannot be the causes of the intense color changes.

3. The dibasic intensely colored salts of the phenolsulfonphthalein series have been made by us and by Lubs and one of us and studied extensively spectrophotometrically. They are shown to be the cause of the intense color changes.

4. These dibasic salts have been shown by conductivity, titration and spectrophotometric methods to be practically solely quinone-phenolate salts possessing the characteristic chromophoric group $—C(.C_6H_4:O)(C_6H_4O^-K^+)$, which is also the seat of the color changes in aurine, phenolphthalein and similar substances. The sulfonphthaleins studied give practically no colorless lactoidal salts.

5. The color of the dibasic salts, and of the tetrabromo- and tetranitrophenolsulfonphthalein, all of which give quinone-phenolate ions, show that the nonionized quinone-phenol, $—C(:C_6H_4:O)(C_6H_4OH)$, is orange or yellow, whereas the quinone-phenolate ion, $—C(:C_6H_4:O)(C_6H_4O^-)$ is intensely colored and is the chief cause of the intense color changes. The

non-ionized quinone-phenolate salt, — $C(:C_6H_4:O)(C_6H_4OK)$, may also be intensely colored, but its concentration is small in dilute solutions.

6. The intense and very sharp color changes in the sulfonphthalein series are far more satisfactory than in the phenolphthalein series because the monobasic salts of the sulfonphthaleins are changed practically quantitatively into the deeply colored quinone-phenolate ion, whereas phenolphthalein gives only about 50% of such deeply colored dibasic ion, the other 50% going over into the colorless lactoidal dibasic ion. The tetrachloro-, tetrabromo-, and tetraiodo-phenolphthalein give only about 1% of the colored, dibasic quinone-phenolate ion, the remainder forming colorless dibasic salts. These facts make the phenolsulfonphthalein series of indicators the best yet discovered. The derivatives described by us, and by Lubs and Clark and one of us, have a wide range of useful *P*H values, show very little of the fading characteristic of the phenolphthaleins and their colors are not greatly disturbed by the "salt effects" which we are studying by the spectrophotometric methods.

MADISON, WISCONSIN.

[CONTRIBUTION FROM THE PURDUE EXPERIMENT STATION.]

SOFT CORN—ITS CHEMICAL COMPOSITION AND NITROGEN DISTRIBUTION.

BY GEORGE SPITZER, R. H. CARR AND W. F. EPPLE.

Received November 18, 1918.

Introduction.

The large amount of corn (maize) produced in this country makes one of our greatest and most valuable sources of food, and hence the success or failure of the crop in any year is a matter of great economic importance. The failure of considerable of the corn to mature properly during 1918 led to much speculation as to the feeding value of soft corn, or to state it another way, the question "What is soft corn?" was often asked. One publication[1] has answered the question in part by stating that very soft corn contains 65% of water (rare) and ranges down to 25%, which is low enough to allow the corn to be stored in cribs. whereas old corn usually contains about 12% of moisture. It might be inferred from this that soft corn differs from mature (corn) only in the amount of moisture it contains, but the present writers have found characteristic differences in the carbohydrates, proteins and mineral constituents. The idea is prevalent in some localities that soft corn is worthless for feeding purposes, whereas others have succeeded in feeding the wet and therefore often moldy corn to cattle and hogs with profitable returns, no cases of poisoning from the mold having been reported to our knowledge. Thus, evidently, soft corn has a feeding value that, although not to be considered equal to that of the mature corn, is far too great to be ignored. One phase of the corn problem has centered about the drying out of this excess moisture which causes the corn to spoil before it can be used. The other side of the soft corn question has to do with its nature after the excess water has been removed. It is on this part of the problem that the authors have tried to throw light.

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[1] Iowa Expt. Sta., *Circ.* 40 (1917).

In order to get a better understanding of the composition of mature corn, and especially its nutritive deficiencies which have been extensively studied, it may be well to recall briefly the main points of this deficiency noted in the literature.[1] These are,—a low per cent. of ash which contains a high proportion of magnesia and a low calcium content; a comparatively large amount of potassium and phosphorus; less protein than contained in most other grains, and this is largely made up of certain distinct and characteristic proteins, such as zein, globulin and glutelin. The first named is said to be the most abundant protein, but there are lacking 3 amino acids in its formula, two of which (lysine and tryptophane) seem essential to the growth and development of a young animal. The other two, globulin and glutelin, are said to be complete proteins and to yield on hydrolysis all the essential amino acids, Hence they are capable of producing growth, but it is noteworthy that they are not present in sufficient amount in the corn grain to support growth.[2]

Procedure.

In response to numerous inquiries as to what is soft corn, the authors have attempted to get some insight into the composition and the nature of its proteins. In order to carry out the investigation, corn was chosen whose previous history was known. In the samples of Series I the corn was chosen because of its extreme softness and failure to germinate, and because the original moisture was known. Another series, II, was obtained from the Botany Department of Purdue University and represents more matured corn capable of germinating, on which certain studies in plant pathology are being conducted. A third series, III, represents an intermediate grade on which only amide nitrogen and acidity determinations were made. All 3 series were based on shelled corn taken from individual ears. It was the purpose of the writers to compare also the nitrogen distribution of these series of corn with that of mature corn,[3] and if possible to secure data on which qualitative classification can be made as to maturity.

Experimental.

The grain was ground so that the starch, etc., would pass an 80-mesh sieve while the bran layers passed a 40-mesh seive. The method of making the analysis was as follows: 3 g. of the air-dry ground corn was placed in an alundun shell No. R. A. 98. It was dried for 5 hours at 100° and then weighed for moisture. The shell was next placed in a Soxhlet tube and the fat extracted and weighed. The shell and contents when free from ether were extracted with hot 95% alcohol. This extraction continued for 5 hours. The residue from the alcohol extraction was dried and weighed and the nitrogen determined by the Kjeldahl method (zein). After the alcohol extraction the sample was treated with cold water for 24 hours, a stirring machine being used part of the time to extract more thoroughly all of the soluble starch and dextrin. The sample was next boiled to get the starch in solution and a solution of diastase of malt added to convert the starch to sugar—a correction being made for the starch in the malt. The starch was determined as follows: An aliquot of the invert sugar solution was boiled with an excess of Fehling's solution and after cooling, filtered through an asbestos filter; washed with distilled water and the filtrate titrated with standard sodium thiosulfate solution according to modification of Low's method. The weight of dextrose multiplied by 0.90 gives the weight of starch, from which the per cent. was calculated.

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[1] *J. Biol. Chem.*, 18, No. 1 (1914).

[2] Ohio Expt. Sta., *Bull.* 255, Jan., 1913.

[3] THIS JOURNAL, 37, 1778 and 2762 (1915).

After removing all of the starch which was water soluble and converted by diastase, the samples still in the filter shells were next refluxed for 30 minutes with 1.25% sulfuric acid, washed and then boiled for the same length of time with 1.25% sodium hydroxide solution. Washing and filtering by this means was simpler than by the official method. This method also prevents a possible loss in filtering. The fiber was then dried and weighed, burned and the shell[1] weighed again. The ash determination was made on the original sample.

A new sample was taken on which the degree of acidity was determined.[2]

Another 5 g. sample of each corn was hydrolyzed for 16 hours with 20% hydrochloric acid and treated according to the Van Slyke method for the determination of acid-insoluble melanin, lime melanin, ammonia nitrogen, monoamino acids, and diamino acids.

The results of the analysis of Series I are given in Table I.

The data for the more mature corn (Series II) are given in Table II.

Amide Determination.

Mature corn has usually been considered nearly free from amides, but this could hardly be expected to be true of soft corn. The method used in making the determinations was a modification of the Stutzer process as developed by Blish.[3]

One part of finely ground corn and 20 parts of water were shaken frequently for 12 hours. Fifty cc. of the filtered solution was then taken and 25 cc of 0.1 *N* sodium

[1] The shells mentioned are very porous and filtration takes place rapidly.

[2] Dept. Agr., Bur. Plant Ind., *Bull.* 102, Jan., 1913.

[3] *J. Biol. Chem.*, 33, 55 (1918).

TABLE I.

Composition and Nitrogen Distribution of Corn. Series I.

Yellow dent variety. Sample No.	Total nitrogen. %.	Insoluble melanin. %.	Lime melanin. %.	Ammonia nitrogen. %.	Monamino acids.	Diamino acids.	Protein. % N × 6 25	Moisture.	Fat.	Water sol. starch. Dextrin. %.	Normal starch *via* diastase.	Total starch *via* acid hydrol.	Pentosans, etc., by difference.	Crude fibre. %.	Ash. %.	Acidity. Degrees.	Water loss from ear. %.
2	1.74	0 099	0.059	0.188	0.997	0.199	10.97	8.81	2.27	2.03	38.07	...	31.40	4.35	2.10	64.8	62.50
3	1.59	0 090	0 061	0.185	1.10	0.179	9.93	9.22	1 96	2 64	38.09	...	32.49	4.29	1.90	54.4	58.33
4	1.55	0 092	0 051	0.179	1.03	0 210	9.62	8.95	1.44	1.70	46.62	...	24.17	5.43	2.07	61.2	56.25
5	1 94	0 101	0 048	0 274	1.36	0.145	12.13	9.03	1.83	2 03	37.09	...	32.37	3 45	2.20	41.6	53.33
6	1.45	0.087	0.078	0 213	0.99	0 104	9 06	8.09	2.00	2.22	49 05	...	22.13	5.25	1.89	58.8	52.85
7	1.63	0 117	0 068	0 241	1 09	0 135	10.19	8.90	2.02	2 04	47 34	...	21.32	6.20	2.14	44.0	52.38
8	1.75	0.101	0.089	0 230	1.05	0 157	11.00	8 46	3.49	1 04	42.71	...	27.03	4.13	1.68	48.8	50.00
9	1.33	0 082	0.089	0 170	0 963	0 090	8.31	8.23	2.53	3 88	39.04	...	30.75	5.58	2.19	54.4	44.40
11	1.65	0 070	0 089	0.260	1.04	0 202	10 33	8.02	3.33	1.62	41 73	...	26 30	6 48	1 65	36.0	42.85
12	1.41	0 080	0.089	0 179	0.903	0 208	8.79	7.53	3.20	3.84	43.45	...	26.68	4 86	1.90	53.2	42.80
13	1.37	0 078	0 087	0.176	0 908	0 179	8.53	7.40	2 38	4.16	49.30	...	21.12	5.21	1.92	33.2	42.80
14	1.32	0.070	0 068	0 200	0.870	0.204	8.27	7.33	3.20	3.44	42.46	...	28.72	4 66	2.11	66.4	41.66
15	1.54	0 063	0 068	0 260	0.963	0.170	0.963	8.93	2.22	2.42	50.52	...	20.26	3 91	2.22	60.8	40.92
16	1.52	0.079	0 078	0 207	0.986	0.213	0 950	8 93	2.42	2.28	39 04	...	29 99	5 62	2.01	47.2	37.50
17	1 42	0 087	0.089	0.193	0.903	0 190	8 88	8.72	2.25	2.55	46.37	...	24.38	4.84	1 90	49.6	37.50
18	1 39	0 070	0 078	0.179	0.990	0 190	8 71	8.88	2 49	3.10	...	...	...	3.58	1.81	41.6	36 66
19	1.22	0 068	0 066	0.213	0.740	0 175	7 61	8.49	2.26	3.89	44.90	...	26.08	4.56	1 59	..	33.31
20	1.23	0.067	0.056	0.179	0 790	0 177	7 66	8.41	2 16	3.57	52.22	...	20.22	4.17	2.06	43.2	...
21	1.96	...	...	...	...	.	12.25	8.28	2.74	3.62	43.20	...	22.28	5.56	1.74	70 0	...
a	1 69	..	...	...	..	...	10 54	7.26	4.70	0.72	50.80	...	15.24	2 59	1.65	..	...
b	1.51	...	..	...	. .	...	9.45	7.66	3.96	1.21	50.24	...	23.11	2.72	2 36	.	...
c	1.92	...	...	...	. .	..	11.99	7.09	3 12	0.45	49.96	...	20 64	4 39	2.40	..	...
d	2.07	...	...	...	...	...	13.68	11.00	2.30	0.82	46 31	..	18.35	5 08	2 32	..	...
e	1.44	...	...	...	...	...	8.96	10.56	1.62	1.10	48.08	...	26.96	2.72	2.33	..	...
149	1.48	0.090	0 038	0.220	0.95	0.161	9.27	5.37	3.56	4.12	51.50	76.28	...	3.23	1 33	..	...
148	1.47	0.089	0.042	0 229	0.994	0.188	9.19	5.47	3.66	3.62	50.52	75.42	...	2.77	1.58	..	...
141	2.02	0.116	0.046	0.294	1.33	0.245	13.50	0.274	3.14	1 08	51.45	76.28	...	2.73	1.87	..	. .
Average	1.58	0.085	0.068	0.212	0.998	0.178	9.92	8.06	2 67	2.40	45 77	...	24 87	4 38	1.95	100.02 (Total)	..
In per cent. of total nitrogen		9.68		13.41	63.16	11.26											

TABLE II.
Composition and Nitrogen Distribution of Corn of Series II.

Variety of corn.	Sample No.	Total nitrogen. %.	Insoluble melanin. %	Lime melanin %.	Ammonia N.	Monoamino acids.	Diamino acids.	Protein N × 6 25	Moisture. %.	Fat	Water soluble starch Dextrins. %	Normal starch via "diastase"	Total starch via acid hydrol.	Pentosans, etc., by difference.	Crude fibre %	Ash. %	Calorific value. Cal/Gm.
90 day corn.	8.03	1 35	0 077	0 049	0 196	0 943	0 095	8 44	7 80	3 65	3 20	50 11		22 99	2 53	1 46	. .
	7 97	1 62	0 082	0 053	0 234	1 107	0 157	10 13	6 37	3 92	1 67		74 03		1 82	1 55	.
	5 05	1 89	0 095	0 042	0 266	1 28	0 207	11.81	6 53	4 84		45 97	74 03	26 95	2 47	1 43	42 67
	1.51	1 98	0 107	0 053	0 267	1 22	0 242	11 76	6 96	2 27	4 69	50 64		19 70	2 37	1 66	
Leaming	8 34	1.92	0 110	0 046	284	1 23	0 225	11 99	8 03	4 30	3 35	50 50		18 17	2 36	1 30	.
	7.05	1 82	0 098	0 053	0 252	1 23	0 213	11 37	5 75	4 55	1 08	46 35	74 13	26 36	2 70	1 84	42 04
	6.83	1 76	0 082	0 053	0 250	1 24	0 180	11 03	4 75	4 68	4 39		76 28		2 63	1 42	
Yellow dent.	8.35	1 91	0 089	0 042	0 255	1 30	0 223	11 90	3 87	5 54	1 66	50 63	75 42	22 44	2 53	1 43	4354
	8.19	1 64	0 084	0 042	0 220	1 17	0 158	10 24	6 96	5 08	1 74	49 45	75 42	21 65	2 17	2 71	4243
	8.10	1 58	0 107	0 046	0 217	1 20	0 154	9 29	6 77	4 64	1 42	46 35	73 71	27 07	2 36	1 60	
	8 12	1 64	0 086	0 042	0 238	1 154	0 157	10 25	6 41	3 49	1 17		77 71		2 05	1 40	
	1 55	1 74	0 084	0 046	0 249	1 24	0 179	10 89	5 35	5 27	2 01		75 85		1 58	1 61	.
	6 96	1 65	0 086	0 038	0 230	1 14	0 158	10 28	7 32	3 82	1 17		79 20		1 83	1 23	.
	7 04	1.95	0 088	0 056	0 294	1 35	0 202	12 16	4 79	5 15	4 12		73 71		2 86	1 89	.
Johnson Co. White	2 45	1 87	0 084	0 038	0 266	1 298	0 187	11 68	3 75	3 83	1 16	42 80	71 40	29 92	2 23	1 30	
	3 44	1 40	0 082	0 042	0 210	1 002	0 102	8 75	7 55	5 10	1 74	46 94	75 32	26 34	2 25	1 33	
	2 51	1 67	0 083	0 042	0 241	1 20	0 140	10 41	7 41	4 70	1 33	46 35	76 28	25 80	2 80	1 33	
	2.26	1 36	0 101	0 042	0 199	0 931	0 098	8 49	5 50	4 30	1 08	45 78	75 22	30 15	2 90	1 61	
Average		1 702	0 090	0 046	0 242	1 18	0 171	10 60	6 21	4 28	2 17	47 65	75 18	24 80	2 36	1 56	—99 63 (Total)
In per cent. of the total nitrogen.....			8 0		14 23	69 41	10 58										

hydroxide solution was added followed by 27 cc of 0.1 *N* cupric sulfate solution. The precipitate was later filtered off and the nitrogen determined in the filtrate by the Kjeldahl method.

In some of the samples the precipitate was also analyzed, but the amount of nitrogen contained was so constant that it was not considered worth while to continue that work.

Protein Separation.

There seems to be some uncertainty in the literature concerning the amount of the individual proteins making up whole corn. No data on a considerable number of ears of corn have come to the writer's attention. In view of this it was thought best to make a study of the amount of corn protein soluble in some of the various solvents. A 10% solution of sodium chloride was used to extract the globulins, albumens and proteoses. They were allowed to stand 72 hours and frequently shaken.

TABLE III

PROTEIN DISTRIBUTION, SERIES I.

YELLOW DENT VARIETY

Sample No	Total N. %	Zein as % of total protein	Globulins, etc., as % of total protein.	Amide as % of total N	Prot. sol. in 10% NaCl % of total protein.	Glutelin as % of total protein.
2	1.74	20.00	22.64	17.70	40.34	39.66
3	1.59	14.68			33.85	51.47
4	1.55	15.00	26.47	17.29	43.76	41.24
5	1.94	26.68	17.54	9.00	26.54	52.78
6	1.45	17.37	24.29	20.08	44.37	38.26
7	1.63	26.32	16.56	17.17	33.73	39.95
8	1.75	20.91			38.56	41.53
9	1.33	26.88	23.64	16.82	40.46	32.66
11	1.65	26.00	21.99	7.96	29.95	44.05
12	1.41	16.15	31.47	16.48	48.95	35.90
13	1.37	18.39	27.35	15.50	42.85	38.76
14	1.32	27.27	25.63	17.80	43.43	29.30
15	1.54	21.51			34.94	43.55
16	1.52	17.17			36.94	44.89
17	1.42	19.36	28.62	13.40	42.02	38.62
18	1.39	22.80				..
19	1.22	20.00			49.89	30.11
20	1.23	16.76	26.54	15.55	42.09	41.15
21	1.96	20.71			39.39	39.90
(*a*)	1.69	24.05	11.68	19.47	31.15	44.80
(*b*)	1.51	22.80	20.98	11.56	32.54	44.66
(*c*)	1.98	23.33	17.56	9.25	26.81	49.86
(*d*)	2.07	30.24		.	27.13	42.63
(*e*)	1.44	24.00			27.62	48.38
149	1.48	21.11	28.12	21.28	49.40	29.49
148	1.47	28.57	29.80	16.72	46.52	24.91
141	2.02	29.81	13.93	8.35	22.28	47.91
Av.	1.58	22.14	23.04	15.08	37.52	40.63

TABLE IV.

Protein Distribution, Series II.

Variety of corn.	Sample No.	Total N. %.	Zein as % of total protein.	Globulins, etc., as % of total protein.	Amide as % of total N.	Prot. sol. in 10% NaCl. % of total protein.	Glutelin as % of total protein.
90-Day corn..........	803	1.35	23.48	...	..	...	34.58
	797	1.62	34.87	25.77	4.83	30.60	34.53
	505	1.89	25.66	...	..	27.20	47.14
	151	1.88	22.08	...	..	30.82	47.10
Leaming............	834	1.92	38.65	16.74	4.06	20.80	40.55
	705	1.82	35.66	...	..	28.17	36.17
	683	1.76	23.07	22.50	5.70	28.20	48.73
Yellow dent.........	835	1.91	36.15	24.80	3.84	28.64	35.21
	819	1.64	38.66	21.52	5.43	26.95	34.39
	810	1.58	29.49	21.52	6.40	27.92	42.59
	812	1.64	27.86	...	..	25.95	46.97
	155	1.74	32.18	...	..	..	...
	696	1.65	22.91	...	..	30.05	47.04
	704	1.95	27.28	18.30	6.95	25.25	47.47
Johnson Co. white....	245	1.87	23.42	..	..	26.55	50.03
	344	1.40	27.00	21.33	5.55	26.88	46.12
	251	1.67	36.64	22.03	4.67	26.70	36.66
	226	1.36	24.36	..	..	29.20	46.44
Av....................		1.702	29.41	21.61	5.27	27.49	42.45

TABLE V.

Amide Nitrogen and Acidity Content, Series III.

Sample No.	Total N. %.	Amide N as % of total N.	Degree of acidity.
41....................	1.52	8.80	30.4
42....................	1.46	9.58	23.2
43....................	1.79	11.70	37.2
44....................	1.65	8.12	22.8
45....................	1.33	5.88	..
46....................	1.61	7.64	22.8
47....................	1.69	8.71	37.1
48....................	1.29	10.40	22.4
49....................	1.76	8.54	41.8
50....................	1.34	8.58	19.6
51....................	1.59	9.17	35.6
52....................	2.05	5.17	35.6
53....................	1.51	6.66	34.8
54....................	1.54	9.09	32.8
55....................	1.25	9.02	30.4
56....................	1.56	8.27	15.2
57....................	1.68	15.60	36.0
58....................	1.73	6.12	27.2
59....................	1.58	8.17	30.4
60....................	1.53	6.20	31.6
Average...........	1.57	8.57	

TABLE VI
Summary of Tables.

	Normal corn	Series I	Series II	Series III.
Protein % N × 6 25	10 1	9 92	10 60	9 81
Per cent of total melanins	9 78	9 68	8 00	
Ammonia N, % of total N	12 53	13 41	14 23	
Monoamino acids, % of total	63 43	63 16	69 41	
Diamino acids, % of total	15 86	11 26	10 58	.
Zein, % of total	41 00	22 14	29 41	..
Globulins, etc, % of total	22 00	23 04	21 61	
Amide nitrogen, % of total		15 08	5 27	8 57
Glutelins, % of total	31 00	40 63	42 54	.
Moisture, %	10 50	8 06	6 21	
Fat	5 00	2 67	4 28	
Water-soluble starch and dextrine	3 38	2 40	2 17	
Normal starch by diastase	42 50	45 77	47 65	
Total starch by acid hydrolysis	71 95		75 18	.
Pentosans, etc, by diff	24 87	24 80	.	.
Crude fiber, %	2 00	4 38	2 36	.
Ash, %	1 50	1 95	1 56	

The amides were also extracted by this solvent but were deducted in calculating the globulin, etc. Determinations were made of the per cent. of the total protein soluble in 0.05 *N* sodium hydroxide solution after standing at room temperature for 72 hours with frequent shaking, and also after heating for one hour in an autoclave at 115 pounds, pressure, to rupture the cells It was found that about 8% failed to go into solution previous to heating. The salt solution was heated under pressure in the same way but no increase in soluble nitrogen could be detected. The portion of the protein soluble in alcohol (zein) was determined as previously described. This protein was found present in smaller amount than has been reported by others, and much less was found to be present in the soft corn than in the more matured of Series II. The results of this work are recorded in Table III for Series I and Table IV for Series II.

Discussion.

It will be noted from the tables that there is a wide range of corn classed as soft corn and that the composition varies considerably among both mature and immature ears. Much of the soft corn of 1917 had been planted 130 days or more and so had had time to mature, but did not advance because of the lack of warm weather during the summer. The composition of the corn is therefore somewhat different from that taken for analysis in the milk, glaze, dented and maturity stages as previously reported from this station.[1]

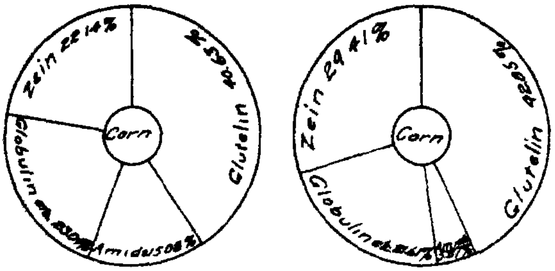
Referring to the summary, Table VI, Series I which represents the most immature corn, shows that the nitrogen content is not greatly af-

[1] Purdue Expt. Sta, *Bull.* 175 (1914).

fected by degree of maturity, as it differs less than 0.2% from that of normal corn. A considerable part of the nitrogen in soft corn is present as amide, however, and evidently has been formed almost entirely at the expense of the zein. There are few data available on the amount of zein in widely selected samples, while that reported is on corn very high in nitrogen (2 33%) and hence may not represent the normal distribution of proteins. Zein is of much interest from a feeding standpoint, because it is an incomplete protein and its presence makes a corn less desirable from a nutritional standpoint. From the analysis of all the samples it would seem that glutelin is the most abundant protein in corn, with zein next and globulin last. The amide or non-protein nitrogen content, and the acidity in soft, moldy corn are quite high, as might be expected and from data presented on the 3 series it would appear the amide nitrogen can be taken as a basis on which maturity may be determined averaging 5.27 to 8.57 to 15.08 for Series II, I, III, respectively. These figures actually approximate the correct grading of the three lots as to maturity.

Considering now the other deficiencies in soft corn as shown in Table VI the low fat content of Series I is the most noticeable feature for it is only about half that of normal corn. It was believed that the amount of true starch as determined by the diastase method would show a considerable deficiency in Series I but this did not prove to be the case. As expected the amount of crude fiber was found to be large and the ash content high. Some combustion determinations were also made and it was found that the difference between the best and the poorest samples was less than 200 calories. Hence, no further work was done in determining the calorific value of the different grades of corn.

Series I. Series II.



Soft Corn. Mature corn.

Protein Distribution.

Summary.

1. The percentages of normal starch and nitrogen-free extract appear to be higher in soft than in mature corn.

2. The formation of protein and carbohydrates apparently go on un-

interruptedly during the growth of corn, while the fat seems to be formed last.

3. The calorific determination is of little service in determining the value of corn for feeding purposes.

4. The acid-hydrolyzed proteins do not reveal any unusual features. The diamines are lower than results reported by others, whereas the monoamines of nearly matured corn are higher, but this is not significant in the present research.

5. The total nitrogen of soft corn is only slightly lower than that of mature corn, but the amide nitrogen is much higher.

6. The amide nitrogen, together with the degree of acidity, may serve as a basis for grading corn. Moldy corn contains a large amount of nitrogen in the amide form.

7. Glutelin is the most abundant protein in corn, zein is next, and globulins, albumens, etc., are present in smallest amount.

8. Since zein appears to be present in smaller amount in soft than in mature corn, and since glutelin, globulins, albumens, etc., are present to about the same per cent. in both mature and soft corn, it would seem that zein is formed last, and amide is formed at the expense of zein.

LAFAYETTE, INDIANA

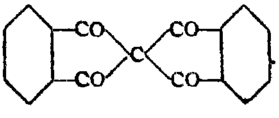
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE COTTON COLLEGE, GAUHATI.]

DIKETOHYDRINDENE. III.[1]

BY ANANDA KISORE DAS AND BROJENDRA NATH GHOSH.

Received April 23, 1919.

It has been shown by one of us with Sastry[2] that the methylene hydrogen atoms in 1,3-diketohydrindene are very reactive, since they condense readily with aromatic aldehydes giving benzylidene derivatives. This led us to think that diketohydrindene could readily condense with anhydrides, such as phthalic anhydride, to give compounds of the type



(I)

Preliminary experiments were therefore conducted, and it was found that the compound obtained was different from the ones noted in the literature. Thus it was noted that Carmelo Marchese[3] had condensed phthalic anhydride and diketohydrindene in the presence of acetic anhydride, and that the product gave an intensely red solution with alkaline hydroxides. He gives as its formula

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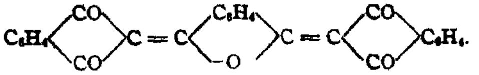
[1] For Parts I and II see *Trans. Chem. Soc.*, 107, 1442 (1915) and 109, 175 (1916).

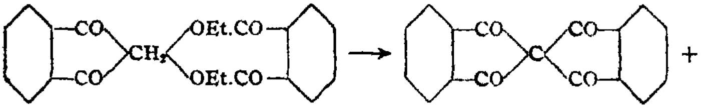
[2] *Trans. Chem. Soc.*, 107, 1442 (1915).

[3] *Gazz. chim. ital.*, 37, 303–309 (1907).


(II)

The compound we obtained by condensing diketohydrindene and phthalic anhydride in the presence of conc. sulfuric acid, though it melts at nearly the same temperature as the compound of Marchese, is different in other respects; for example, it is not at all soluble in alkaline hydroxide; from nitrobenzene solution it separates immediately in golden yellow plates, whereas his substance is very soluble in nitrobenzene and comes out, in well-defined needles, only on the addition of alcohol; on boiling with aniline our substance separates unchanged and contains no nitrogen; his substance did not separate from aniline, but on pouring the solution into dil. sulfuric acid a black crystalline compound precipitated, differing from the original substance, but not containing any nitrogen. The exact chemical nature of his substance we do not know; it appears to be some degradation product of the original compound. It is, however, a pure substance, as it gives a definite melting point. But we do not know whether decomposition was effected by the aniline or by the sulfuric acid, and so we cannot state definitely the way in which the molecule has been changed.

From the percentage composition we find at any rate that the substance obtained by condensing the phthalic anhydride and diketohydrindene is not the same as given in Formula I. Having failed to prepare the desired compound in this way, we next tried the action of sodium alcoholate on a mixture of diketohydrindene and diethyl-phthalate on the assumption that the reaction would proceed in the following manner:



But after conducting the reaction as described below, we obtained a substance which resembled in every way benzoyl-β,γ-diketohydrindene obtained by E. Schwerin[1] from ethyl-phthalate and acetophenone. It is probable that the desired compound was obtained, but was not stable under the conditions of the experiment, because of the number of carbonyl groups attached to one carbon atom, and so hydrolyzed to *o*-carboxy-benzoyldiketohydrindene, which again decomposed, giving off carbon dioxide with the production of benzoyl-diketohydrindene. In this reaction a little anhydro-*bis*-diketohydrindene[2] is also formed which can easily be separated from the benzoyl-diketohydrindene by the slight solubility of the former compound in alcohol. That it is the *bis* compound has been proved by its properties as well as by analysis.

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[1] *Ber.*, **27**, 104–114 (1894).

[2] Wislicenus and Kotzle, *Ann.*, **252**, 76, 77 (1889).

We also tried the condensation of phthalic anhydride, benzoic anhydride and succinic anhydride with diketohydrindene, these 3 being taken to represent 3 classes of anhydrides. Phthalic anhydride is a typical closed chain aromatic anhydride; benzoic anhydride has an open chain, and succinic anhydride is a closed chain aliphatic anhydride. The conditions of the experiment were kept practically uniform. The 3 substances obtained resemble each other very much in their percentage compositions, but their properties, such as solubilities in various solvents, are different. They are, without exception, difficultly soluble in all ordinary solvents; they do not form anilides; they are very high melting and complex substances. It is true that two molecules of diketohydrindene first condensed to form anhydro-*bis*-diketohydrindene[1] and then the anhydro substance condenses with the respective anhydrides giving complex substances. It has been proved that the same substance is produced by condensing phthalic anhydride with either diketohydrindene or anhydro-*bis*-diketohydrindene.

Experimental.

2-Benzoyl-1,3-diketohydrindene.—0.7 g. of sodium was dissolved in 20 cc. of absolute alcohol, the solution was thoroughly cooled, and to it was slowly added 2 g. of 1,3-diketohydrindene dissolved in a little alcohol. The mixture turned red, 3.1 g. of diethyl-phthalate was then added to it and the whole boiled under a reflux condenser on a water bath for 5 to 6 hours. The intensely red solution, after standing overnight, deposited a small quantity of solid, which dissolved on the addition of water. A current of carbon dioxide was passed through the solution, which was then extracted with ether. The aqueous solution on acidification gave a crystalline solid which crystallized from alcohol in almost colorless needles. This was shown by analysis, melting point, and other properties to be benzoyl-diketohydrindene obtained by Schwerin.[1]

Calc: C, 76.8; H, 4.0. Found: C, 76.9; H, 4.

To confirm this we also prepared the semicarbazone by boiling an alcoholic solution with an excess of an aqueous alcoholic solution of semicarbazide hydrochloride containing sodium acetate. A colorless substance precipitated.

Subs., 0.0985: N_2 (29° and 760 mm.), 10 cc. Calc. for $C_{17}H_{13}O_3N_3H_2O$: N, 12.3. Found: 12.2.

In this reaction a small quantity of a yellow crystalline substance, almost insoluble in alcohol, was obtained. This was crystallized from acetone, and, as indicated by its melting point, and by analysis, as well as by other properties, was evidently anhydro-*bis*-diketohydrindene, obtained by Wislicenus and Kotzle.

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[1] *Loc. cit.*

Calc.: C, 78.8; H, 3.6. Found: C, 78.4; H, 4.0.

Condensation of Diketohydrindene and Phthalic Anhydride.—2 g. of diketohydrindene and 2.2 g. of phthalic anhydride were mixed and 30 cc. of conc. sulfuric acid added. The mixture was warmed to 50–60° on a water bath, forming a dark brown solution. The heating was continued for an hour, and the mixture after being cooled was poured into cold water when a yellow mass separated. This was dried on porous earthenware, and then recrystallized from nitrobenzene.

Subs., 0.1983: CO_2, 0.6077; H_2O, 0.0669.
Calc. for $C_{25}H_{12}O_3$: C, 83.3; H, 3.3. Found: C, 83.5; H, 3.7.

This substance crystallizes in fine, lustrous flakes, melting at 320° (uncorr.). It is soluble in hot nitrobenzene and aniline; sparingly soluble in xylene, and insoluble in alcohol, acetone, benzene, petroleum ether, and in sodium hydroxide solution. It does not form an anilide. It dissolves in conc. sulfuric acid, giving a brown solution which is not fluorescent. The solution in aniline has a green color. The substance does not sublime on heating.

Anhydrophthalyl-*bis*-1,3-diketohydrindene, II.—This substance was prepared by the method given by Marchese.[1] It was mixed with an excess of aniline and the mixture boiled under a reflux condenser for about an hour. The solution thus obtained was cooled and poured into dil. hydrochloric acid. The black substance which separated was recrystallized from dil. alcohol, giving black prisms which, when heated in a capillary tube, contracted at about 85° and melted to a clear liquid at 110°. The substance is not an anilide because it does not contain any nitrogen.

Subs., 0.1017: CO_2, 0.3029; H_2O, 0.0139.
Calc. for $(C_8H_6O)_x$: C, 81.2; H, 5.08. Found: C, 81.2; H, 5.3.

Condensation of Diketohydrindene and Benzoic Anhydride.—A mixture of 1.46 g. of diketohydrindene, 2.26 g. of benzoic anhydride, and 25 cc. of conc. sulfuric acid, was heated on a water bath at 50° for an hour and then poured into cold water. The substance which separated was collected, washed, dried, and recrystallized from nitrobenzene.

Subs., 0.1504: CO_2, 0.4603; H_2O, 0.0478.
Calc. for $C_{25}H_{12}O_3$: C, 83.3; H, 3.3. Found: C, 83.4; H, 3.5.

The substance crystallizes in golden yellow needles which sublime on heating and melt to a clear liquid only at a very high temperature (above 320°). It is more soluble in nitrobenzene than the previous compound and separates only slowly from its solution.

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[1] *Loc. cit.*

Condensation of Diketohydrindene and Succinic Anhydride.—A similar product was obtained by condensing 1.5 g. of diketohydrindene and one g. of succinic anhydride in presence of 30 cc. of conc. sulfuric acid, and warming the mixture for one hour at 50°. On pouring into water a greenish mass was obtained, which was recrystallized from nitrobenzene. The substance separates very slowly, requiring sometimes the addition of alcohol. It does not melt even at 316° but sublimes on heating, and is insoluble in alcohol, acetic acid, acetone and benzene. Its solution in aniline is greenish in color, and the substance obtained by pouring the solution into dil. hydrochloric acid did not contain any nitrogen.

Subs., 0.1245 CO_2, 0.3776, H_2O, 0.0391.

Calc for $C_{22}H_{10}O_3\ H_2O$ C, 83.1, H, 3.3 Found C, 82.7, H, 3.5

Our thanks are due to Principal Südmersen for the kind interest he has taken in the work.

ASSAM, INDIA

[CONTRIBUTION FROM THE STANFORD MEDICAL SCHOOL.]

A METHOD OF TISSUE ANALYSIS: APPLIED TO THE POSTERIOR AND ANTERIOR LOBES OF CATTLE PITUITARIES.

BY C. G. MACARTHUR.

Received April 24, 1919

The cattle pituitaries used in these experiments, were obtained from a local packer. They had been collected over a period of several days and kept frozen until ready for analysis. After freeing the pituitary from bone, connective tissue, fat, etc., it was separated into anterior and posterior lobes. Exactly 10 g. of skin-free, ground material from each lobe was weighed in conical flasks and treated as described under "Method"

Method of Analysis.

The method of analysis used is based on the separation into proteins, lipins and extractives that has already been proven satisfactory.[1] The original method has been simplified, extended to new determinations, and been made available for much smaller amounts of material. The amounts of tissue usually used (10 g.) are probably the most satisfactory, but most of the determinations described can be carried out on 2 g., though with somewhat less accuracy. It will be noticed that the new methods for small quantities are applied in some cases. In others it will be seen that the usual quantitative methods are made available and accurate by decreasing the volume of solutions used to about $^1/_{10}$, avoiding transference of material whenever possible, often by use of centrifuge tubes, and the titration of the material in these smaller volumes with 0.01 *N* instead of 0.1 *N* solutions. It is believed that in this way the usual accuracy is maintained, though only small amounts are actually estimated. Obviously greater care must be used in gradation when smaller apparatus is used. Only redistilled organic solvents were employed.

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[1] W. Koch, "Methods for the Quantitative Chemical Analysis of Animal Tissue," THIS JOURNAL, 31, 1329 (1909); M. L. Koch and C. Voegtlin, "Chemical Changes in the Central Nervous System in Pellagra," *Hygienic Lab. Bull.*, 103, 51 (1916).

In the alcohol method used in this investigation, 10 g. of tissue was placed in a 100 cc. conical flask and redistilled alcohol added until the concentration of the alcohol in the solution was about 80%. The corked flask was then allowed to stand in a dark place for several weeks, although the time could be shortened when necessary by repeated heatings. Then on each of several successive days the mixture was brought just to the boiling point 3 or 4 times. Finally the hot alcohol was decanted through a weighed, paper-lined, perforated crucible into a weighed 75 cc. beaker. More alcohol was added to the residue in the flask, the mixture heated and decanted as before. This was repeated 4 times. The residue was then allowed to stand overnight in ether, warmed several times and decanted, after which it was transferred to a glass mortar, thoroughly ground, and again placed in a flask. The alcohol and ether extractives in the meantime were concentrated on a steam bath.

The residue in the flask was then digested 3 times with about 20 cc. of hot water, and the water extracts decanted through the same weighed crucible into a separate beaker. After concentrating to about 5 cc., enough alcohol was added to make the alcohol concentration 80%. It was heated to boiling until the protein was coagulated, then poured through the crucible, again heated to boiling and poured through crucible into the *first weighed* beaker. The residue was then heated and transferred to the crucible. 95% alcohol was heated in separate beaker and used to wash out the flask, used repeatedly for this purpose, and finally collected in the weighed beaker. By proper manipulation with a glass rod, all of the residue was now in the weighed crucible.

This crucible was suspended in a continuous extractor and extracted with 95% alcohol for 30 hours. The alcohol extract was then transferred to the weighed beaker residue. The residue in the crucible was then extracted 10 hours with chloroform, the extract transferred to the weighed beaker and evaporated carefully to dryness, and dried to constant weight in a vacuum desiccator. This gives the weight of the lipins plus the extractives. The protein residue in the crucible was then heated to constant weight in a 105° oven and kept in vacuum desiccator. The total solids equal the sum of these two weights.

About 40 cc. water was added to the beaker containing the extractives and lipins. After considerable stirring and some time, a homogeneous emulsion was obtained. This was transferred to a 50 cc. centrifuge tube and $^1/_2$ cc. of hydrochloric acid added with stirring. As soon as the lipins were precipitated, the material was centrifuged and then decanted carefully into a 100 cc. measuring flask (lipin flask) containing about 5 cc. of chloroform. This flask was thoroughly shaken for several minutes, allowed to settle and the watery part added to a second centrifuge tube, centrifuged, and the clear, almost colorless solution of extractives filtered into a 100 cc. measuring flask. The residue in the first centrifuge tube was washed with about 30 cc. of water containing $^1/_4$ cc. of hydrochloric acid. The centrifuged solution was placed in the 100 cc. lipin flask and shaken with the chloroform, treated just as the original solution, and finally added to the 100 cc. extractive flask. The residue in the tube was washed once more with 30 cc. of water containing $^1/_4$ cc. of hydrochloric acid and treated as before.

The material in the extractive flask was made up to 100 cc. Aliquots of this solution were used later for the various determinations.

The residue in the centrifuge tube was dissolved in a mixture of absolute alcohol and chloroform (approximately 10 to 1), and added to the lipin flask. All the apparatus used for the precipitation of the lipins was washed thoroughly with alcohol-chloroform mixture and the latter transferred to the lipin flask and diluted to the mark with absolute alcohol. If the proper amounts of alcohol, chloroform and water (not much of the last two) are present, a clear solution is obtained.

Extractives.

By evaporating 30 cc. (or another aliquot part) of the extractives to dryness in weighed crucible or dish and bringing to constant weight in a vacuum desiccator over calcium chloride, the weight of extractives was obtained. Subtracting the weight of extractives from that of lipins and extractives gave the total weight of the lipins. This same organic and inorganic residue was carefully ignited to constant weight. The ash is not a measure of the inorganic salts alone, and probably the original ions are considerably rearranged; yet it is a helpful determination. This ash was dissolved in warm dil. nitric acid, made to 10 or 25 cc. and part used for the determination of one or more of the following: sodium, potassium, calcium, magnesium, phosphorus, iron (chlorine, sulfur).

Calcium was determined by placing an aliquot part ($^1/_2$) in a centrifuge tube, making slightly alkaline to phenolsulfonphthalein with ammonia, boiling till neutral, then while hot adding slowly one cc. of a solution of 1.25% oxalic acid in 0.25 *N* hydrochloric acid. The mixture was allowed to cool and 0.5 cc. of 20% sodium acetate solution added. After standing overnight this was centrifuged, washed twice by centrifuging with 5 cc. portions of cold water and 2 cc. of 5% sulfuric acid added.

It was then heated and titrated with 0.01 N potassium permanganate solution to a faint pink color.[1]

Magnesium was determined in the filtrate from the calcium determination. This was incinerated with a small amount of sulfuric acid, then transferred with water to a centrifuge tube and precipitated as magnesium ammonium phosphate. After washing with dilute ammonium hydroxide it was dissolved in a few drops of nitric acid. Thereafter the procedure was as in the phosphorus determination given below.

Total nitrogen in the extractives was determined in a 2 cc. portion by combustion with 1 cc. sulfuric acid (and small amount of cupric sulfate) in a good-sized, hard test-tube. It was diluted to 10 cc. in same tube, made alkaline, and the ammonia aerated into 5 cc. of 0.01 N hydrochloric acid.

For **ammonia nitrogen** 10 or 20 cc. of the extractives, after being made *slightly* alkaline with sodium hydroxide, was aerated into 0 01 N hydrochloric acid.

Urea Nitrogen.—The alkaline solution from the ammonia nitrogen determination was then carefully neutralized to litmus and urease added. The mixture was then incubated one hour, made alkaline, and the ammonia aerated into 10 cc. of 0.01 N hydrochloric acid.

Amino Nitrogen.—Five cc. of extractives was evaporated to 2 cc. and the amino nitrogen determined in small amino apparatus.[2]

For **Creatinin** 5 cc. of the extractives was saturated with picric acid and made alkaline with $^1/_2$ cc. of 10% sodium hydroxide as usually stated, and made up to 10 cc. Whether the resulting color is due to creatinin only is doubtful. After 20 minutes it was compared in a colorimeter with a standard made in the same way.

Creatin and Creatinin.—Five cc. of extractives was saturated with picric acid, diluted to 50 cc., boiled for 2 hours down to 5 cc., made up to the required volume and alkalinity as for creatinin, and compared with standard in colorimeter.

Uric acid[3] was determined if any was present by taking a large aliquot part of extractives and evaporating to 5 cc. 2 cc. of silver magnesia mixture was added and the mixture centrifuged. The residue was dissolved in 2 drops of 5% potassium cyanide solution, stirred, and 0.5 cc. of water, 0.5 cc. of phosphotungstic acid reagent, and 2 cc. of 20% sodium carbonate solution added. After making up to 10 cc. it was compared in a colorimeter with standard uric acid solution treated in same way.

[1] J. O. Halverson and O. Bergeim, "Determination of Small Amounts of Calcium Particularly in Blood," *J. Biol. Chem.*, 32, 159 (1917).

[2] D. D. Van Slyke, "The Micromethod for Gasometric Determination of Aliphatic Amino Nitrogen," *Ibid.*, 23, 407 (1915).

[3] O. Folin and W. Denis, "On the Colorimetric Determination of Uric Acid in Urine," *Ibid.*, 14, 95 (1913).

Total extractive sulfur was determined by evaporating 5 (or 10) cc. in a nickel crucible with not more than 0.5 cc. of a 20% solution of potassium hydroxide and sodium nitrate (4-1). (It is also safe to use the magnesia fusion method. See lipin sulfur.) The amount of alkali salts must be kept low, for they interfere with precipitation of benzidine sulfate. When dry, it was heated on electric plate or over an alcohol lamp and finally with sulfur-free or asbestos protected burner if necessary, dissolved in water, transferred to a 25 cc. beaker, made acid with hydrochloric acid, evaporated to dryness, taken up with hydrochloric acid, again evaporated to dryness. The treatment with hydrochloric acid was repeated, and the solution taken up in 2 cc. of water and transferred to a centrifuge tube. Ten cc. of benzidine solution was added and the mixture allowed to stand, after which it was centrifuged and washed 3 times with saturated benzidine sulfate solution. Finally the benzidine sulfate was titrated with 0 01 *N* sodium hydroxide solution.

For **Sulfur as sulfates,** 20 cc. was neutralized, evaporated slowly to about 2 cc., transferred to a centrifuge tube, and made slightly acid with hydrochloric acid. It was then heated in a water-bath and 0.01 *N* barium chloride solution added drop by drop. The end-point was moderately sharp, when a drop did not produce a cloudiness in the clear centrifuged liquid after some time standing. A 0.01 *N* sulfuric acid solution was used to titrate back if necessary. This determination is somewhat tedious, but is the most satisfactory one for small amounts of sulfates.

Neutral sulfur is the difference between total extractive sulfur and sulfate sulfur.

Extractive sugar (+ other copper reducing substances) was estimated by neutralizing 2 cc. of extractive solution in a test-tube. To this was added one cc. of mixed Fehling's solution. This was heated in boiling water for exactly 5 minutes, then placed in ice water for several minutes. Five cc. of 40% sulfuric acid and 5 cc. of 100% potassium iodide were slowly run in and the cold solution titrated immediately with 0.02 *N* thiosulfate solution to faint salmon pink color, with starch as indicator. It is usually best to run one or two tubes on the copper solution and one or two on known sugar solutions of the concentration expected.

Total extractive phosphorus was estimated in 2 cc. after destroying the organic material by heating with 0.5 cc. of sulfuric acid and 3 cc. of conc. nitric in a test-tube. If the sulfuric acid residue was colorless, it was transferred with water to a 15 cc. centrifuge tube, neutralized with ammonium hydroxide, and made slightly acid with nitric acid. To this, the volume of which should be about 5 cc., was added 2 cc. of 50% ammonium nitrate solution, and the mixture was heated to 70° in water, 3 cc. of ammonium molybdate solution added, and allowed to stand at 65°

for 20 minutes. By a judicious use of a rubber tipped rod and a fine spray from a wash-bottle (with occasionally a drop of alcohol) the precipitate was centrifuged satisfactorily. After decantation, it was twice washed with one per cent. ammonium nitrate solution and once with water by centrifuging. An excess of 0.1 *N* sodium hydroxide solution was added with a carefully graduated one cc. pipet (using the same one in the same way for the 0.01 *N* acid value), one drop of phenolphthalein solution added and the solution titrated immediately with 0.01 *N* hydrochloric acid.

For **Phosphates,** ammonium nitrate and ammonium molybdate solutions were added to 2 cc. of extractives in a centrifuge tube at 65°, the mixture centrifuged, washed and titrated as above.

Neutral phosphorus is the difference between total extractive phosphorus and phosphate phosphorus.

Lipins.

An aliquot part of the lipin solution (30 cc.) was evaporated to dryness in a 200 cc. round-bottomed flask and 25 cc. of water and one cc. of concentrated hydrochloric acid added. The contents were refluxed for 30 hours, after which the solution was decanted and filtered into measuring cylinder or flask. The fatty acid residue was again heated with 15 cc. of water and 0 5 cc. of hydrochloric acid for 10 hours, and filtered into same cylinder or flask. After washing the residue a few times with acidulated water, the combined solutions were made up to 40 or 50 cc.

The lipin residue was dissolved in ether or chloroform and evaporated to constant weight in weighed beaker, then dissolved in chloroform and made to 10 cc.

Lipin Residue Nitrogen and Phosphorus.—Two cc. was evaporated and digested with 2 cc. of sulfuric acid and a drop of cupric sulfate until colorless. Water was added, the solution made accurately to 10 cc., and 2 cc. used for the phosphorus determination (see extractive phosphorus above) and 8 cc. used for nitrogen (see extractive nitrogen above).

Lipin Residue Sulfur.—Another 2 cc. was evaporated in a nickel or porcelain crucible with one g. of calcined, washed, light magnesia containing about 0.01 g. of sodium carbonate. When dry it was ignited slowly over alcohol lamp. Fumes should not appear. The heat was gradually increased until the mass was colorless. It was then extracted for $^1/_2$ hour with 10 cc. of water on a water-bath, and filtered. The residue was then extracted 3 times more with 5 to 10 cc. portions of water. To the combined filtrates 0.5 cc. of conc. hydrochloric acid and 0.5 cc. of bromine water, were added, and evaporation carried to dryness. A few cc. of hydrochloric acid was then added, and again the residue was evaporated to dryness. This was repeated and the mass taken up in 3 cc. of water, transferred to a centrifuge tube with 10 cc. of benzidine hydrochloride solution, and after 15 minutes, centrifuged, washed 3 times with water saturated with benzidine sulfate, and 5 cc. of water and 1 drop of phenolphthalein added and the solution titrated hot with 0.01 *N* potassium hydroxide solution.

Amino Nitrogen.—Five cc. of the lipin hydrolysis filtrate was neutralized and evaporated to 2 cc. and the amino nitrogen determined in an amino apparatus.

The total filtrate nitrogen, in another 5 cc. portion, was determined by the usual combustion with one cc. of sulfuric acid and a drop of cupric sulfate solution, and aeration into 10 cc. of 0.01 *N* hydrochloric acid. Phosphorus can be determined in aliquot part following digestion, if desired.

Volatile Amine Nitrogen.—Ten cc. of the filtrate was made slightly alkaline in a test-tube and the ammonia aerated into 5 cc. of 0.01 *N* hydrochloric acid, and the nitrogen calculated as ammonia.

Cholin Nitrogen.—The contents of this test-tube was neutralized and washed into a small flask, evaporated to dryness, and covered with absolute alcohol. The residue was pulverized and allowed to stand till the extraction was complete. It was then filtered and washed several times with hot absolute alcohol; an excess of alcohol solution of chloroplatinic acid was added and the mixture allowed to stand overnight, then centrifuged, and washed with alcohol. The residue was dissolved in water, transferred to a test-tube and the nitrogen estimated in the usual way. The results were expressed as choline nitrogen, although there may be other forms present.

Iodine Absorbed.—Five cc. of the filtrate was evaporated to dryness in a 25 cc. flask, and 2 cc. of chloroform or glacial acetic acid added. Exactly 1 cc. mercury chloride and iodine (Hübl's) solution carefully mixed into this, the mixture shaken and allowed to stand overnight in an icebox. One cc. of reagent was treated in exactly the same way as a blank. Each was then titrated with 0.01 *N* thiosulfate solution. From the data obtained the iodine absorbed by the lipin hydrolysis filtrate was calculated.

Sulfur.—After evaporating 5 cc. of the filtrate to dryness it was digested with 0.5 cc. potassium hydroxide-sodium nitrate fusion solution (or one can use the magnesia fusion, as described under Lipin Residue Sulfur). The organic matter was destroyed and the sulfur estimated as benzidine sulfate as described under extractive sulfur.

Sugar was estimated in 2 cc. of the filtrate as described under extractives; or, after neutralization, by adding 2 cc. of saturated picric acid solution, 2 cc. of 20% sodium carbonate solution, and heating for one hour in boiling water. A known sugar solution of about the same strength was treated in the same way, and the two compared in a colorimeter.

20 cc. of the original lipin solution was evaporated to dryness in a nickel crucible, 5 cc. of potassium hydroxide-sodium nitrate solution added, and the mixture evaporated to dryness on a water bath. It was then taken up in water and again evaporated to dryness, after which it was placed on an electric stove or over an alcohol lamp and heated until white. It was sometimes necessary to take up in water, evaporate and heat a second time. Finally it was taken up in water and made up accurately to 10 cc. or any other convenient volume. 0.5 or one cc. of the above 10 cc. was made acid with nitric acid, and *phosphorus* determined as previously described. This was a check on the acid fusion described below.

Total Sulfur.—Two cc. of this solution was placed in an evaporating dish, an excess of hydrochloric acid added and evaporated to dryness. The residue was dissolved in hydrochloric acid and evaporated to dryness. After repeating this treatment twice, the residue was transferred to a centrifuge tube with a small amount of water and sulfur determined by benzidine method described above.

As a check on this method, another 2 cc. portion was treated with hydrochloric acid, as described, then 5 cc. of water was added, and the solution brought to boiling. 2 cc. of barium chromate solution (4 g. pure barium chromate in one liter of *N* hydrochloric acid) was added and the solution boiled 2–5 minutes, a piece of litmus paper was introduced, then calcium carbonate in excess, the mixture shaken, allowed to stand a few minutes, filtered and washed until the volume of filtrate was 10 cc. To the filtrate was added 0.5 cc. of hydrochloric acid and 0.2 g. of potassium iodide. Titrate with 0.01 *N* thiosulfate solution. It was necessary to check the reagents and it was found best to run a known amount of 0.01 *N* sulfuric acid as a control experiment. All conditions must be kept uniform. Whenever the amount of salts is appreciable, this method is better than the benzidine one (but the results are uncertain in the extractive fraction, for there may be present substances other than sulfates that bring about a liberation of iodine).

Calcium and Magnesium.—Using a 5 cc. portion calcium was estimated as described under extractives. The filtrate from calcium was used for magnesium if present in appreciable quantities.

Cholesterol[1] was estimated in the following way: A small amount of calcium carbonate and anhydrous sodium sulfate was added to a one cc. portion of the lipin solution and the mixture evaporated to dryness in a warm but not hot place. When dry, the residue was extracted several times with 2 cc. portions of warm chloroform. These were filtered into a 10 cc. graduate, and made to 10 cc. Two cc. of acetic anhydride and 0.2 cc. of sulfuric acid was added. The mixture was then shaken and allowed to stand $^1/_2$ hour. One or two mg. of cholesterol, or the amount expected, in chloroform, was treated in same way at the same time. The color of standard was compared with the unknown in a colorimeter.

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[1] W. R. Bloor, "The Determination of Cholesterol in Blood," *J Biol. Chem.*, 29, 437 (1917).

The **iodine number** was found for 2 cc. of the lipin solution by evaporation to dryness, dissolving in 3 cc. chloroform, adding one cc. mercuric chloride iodine solution, allowing to stand in the cold overnight, and titrating with 0.01 N thiosulfate solution.

Lipin Nitrogen.—The organic matter in the residue from 2 cc. of lipin solution was destroyed with one cc. of sulfuric acid and one drop of cupric sulfate solution in large test-tube. The *lipin nitrogen* was determined in the whole sample, after making it alkaline, by aerating the ammonia into 0.01 N hydrochloric acid, or the solution was made up to 10 cc., and 8 cc. used for nitrogen and 2 cc. for phosphorus as described above.

Lipin phosphorus was best determined by digesting one cc. of lipin solution with 0.3 cc. of sulfuric acid and enough conc. nitric acid to make the solution colorless when evaporated until white fumes appeared. When the solution was boiled very slowly so that the nitric acid was not rapidly removed, the organic matter was more quickly destroyed. The residue was taken up in 3 cc. of water, most of the acid neutralized with ammonium hydroxide and the phosphorus determined as described above.

Proteins.

About 0.20 g. of protein material was exactly weighed out in a nickel crucible. Because of the hygroscopic nature of proteins this had to be done very quickly, or better, the weight taken was determined by difference in weighing bottle weights. Water and 5 cc. of the potassium hydroxide and sodium nitrate fusion mixture were added and fusion was completed as described above. The mixture was finally made to 10 cc.

Phosphorus in one cc. was determined as described above.

2 cc. was used for **sulfur** determination by the benzidine method as given under lipin sulfur.

In another 2 cc. sulfur was determined by the chromate method described under lipin sulfur.

Calcium was determined in 5 cc. as described for calcium in extractives.

Chlorine was estimated in one cc. by making it slightly acid with nitric acid in a centrifuge tube adding one cc. of 0.1 N silver nitrate solution, centrifuging and titrating with 0.02 N potassium thiocyanate solution, using ferric ammonium sulfate as an indicator. If desired, the solution in tube can be decanted into flask, the residue washed twice, and the contents of the flask titrated for excess silver.

Nitrogen.—Using about 25 mg. of protein in a test-tube, organic matter was destroyed with sulfuric acid and cupric sulfate as usual. The residue was made alkaline and the ammonia aerated into 0.1 N hydrochloric acid, or made up to 10 cc., and 6 cc. used for phosphorus determination and 4 cc. for nitrogen.

0.25 g. of protein was hydrolyzed in a 300 cc. round-bottomed flask with 20 cc. of 10% sulfuric acid for 25 hours[1]. The completely hydrolyzed solution was made up to 40 cc. and the *total protein nitrogen* determined in two 1 cc. portions in usual way.

The remainder of this solution was filtered through a dry filter into a 50 cc. centrifuge tube, and the nitrogen determined in two more 1 cc. portions. The difference between the two sets was the *insoluble humin nitrogen.* The measuring cylinder (and filter paper) was washed. $^{38}/_{40}$ of the original sample was then in the centrifuge tube. 3 g. of phosphotungstic acid in saturated solution was added, the solution stirred, and let stand overnight. It was then centrifuged, decanted into a beaker, washed twice by centrifuging with 25 cc. portions of 2.5% phosphotungstic acid 5% sulfuric acid solution.

The phosphotungstic precipitate was washed into a large test-tube with about 15 cc. of water, made slightly but distinctly alkaline and the ammonia aerated into 5 cc. of 0.1 N hydrochloric acid. This is the *ammonia nitrogen.*

Barium chloride solution was added in slight excess and the mixture filtered into a 50 cc. measuring flask, washed and made up to volume.

Total nitrogen in 2 cc. and *amino nitrogen* in another 2 cc. were determined, allowing the gas to generate for 30 minutes for complete formation of nitrogen from lysine.

To 20 cc. in small flask was added 5 g. of sodium hydroxide, and the flask was placed in series as for an ammonia determination. It was then heated for 6 hours just to boiling while passing in a very slow stream of air, and thus aerated into 5 cc. 0.1 N hydrochloric acid. During the last hour it was boiled and aerated more rapidly. The result was calculated as *arginin nitrogen.*

The phosphotungstic filtrate was treated with a slight excess of finely ground barium hydroxide, filtered and washed thoroughly. This solution should always be tested for ammonia by aeration, because some phosphotungstic acids do not precipitate all of it. The slightly alkaline solution was made slightly acid with sulfuric acid and evaporated to about 25 cc. filtered and washed into a 50 cc. centrifuge tube. 0 3 N barium hydroxide solution and 0.3 N sulfuric acid were alternately added until approximately no precipitate formed on adding a drop of either. After centrifuging, a drop of either reagent very soon formed a precipitate. The removal of the barium and sulfate ions was continued alternately, adding and testing with 0.1 N barium hydroxide solution and 0.1 N sulfuric acid. When this point was reached, one or two drops of either reagent produced a distinct cloudiness in a few minutes. Some patience was required to get this point correctly. The solution was then filtered into a 50 cc. measuring flask, washed, made up to volume, a few drops of toluene added, and the whole shaken.

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[1] D D. Van Slyke, "Improvement in the Method for Analysis of Proteins by Determination of the Chemical Groups Characteristic of the Different Amino Acids," *J. Biol. Chem.*, 22, 281 (1915).

A 2 cc. portion of this filtrate was used for *amino nitrogen* determination.

The *total nitrogen* in this fraction was determined by means of a sulfuric acid combustion, as described above.

A 5 cc. portion was used for *amino acid nitrogen* by the copper method.

Another 5 cc. was used for the formol titration.

Though not definitely proven to be correct, a few data indicate that the aspartic and glutamic acids can be estimated by titrating 10 cc. to a faint pink with phenolphthalein, running a blank with an alanin solution of similar concentration to that of amino acids present. Or one can precipitate them as calcium salts and estimate the nitrogen. It should be possible to estimate tyrosin in this fraction with the phosphotungstic molybdate reagent by comparison with a tyrosin standard.

The soluble humin nitrogen was calculated by adding the total nitrogen found in the phosphotungstic precipitate and filtrate, including the ammonia + insoluble humin nitrogen, and subtracting this from the total nitrogen before precipitation of the basic nitrogen. Obviously errors in previous determination collect in this estimation.

General Discussion.

There are several questions of physiological importance upon which an analysis of the pituitary may shed light. The glandular anterior lobe has its origin in the alimentary canal, while the nervous posterior lobe originates from the same structure as the nervous system. It is natural, then, to ask to what extent have the differences due to independent origin been preserved; and how far have these original differences been changed by juxtaposition and coöperation in function? It might be expected that the posterior lobe would be more nearly like the nervous system than like the ailmentary canal in amounts of the various chemical substances present and that the anterior lobe would resemble more closely the alimentary canal.

It is necessary to add that because of the early union of the two portions, it is probable that the material from which they were formed had not yet assumed many chemical differences. In this case the peculiarities in the chemical nature of the two lobes would be of a common development. Even then, however, there must have been some potential or actual differences at the time of union that would persist in making the anterior lobe more like the alimentary canal tissue and the posterior like nervous tissue.

It is pertinent to ask, too, what the data show in regard to the origin or presence of the active principles of the pituitary. There should be indications of such active compounds if present in appreciable quantities. Also, what tissues or what kinds of tissues do the lobes of the hypophysis most nearly resemble? There is some evidence, for example, that the anterior lobe is similar in function to the thyroid; therefore it may be similar in composition. There should also be comparison with other glands, especially those of internal secretion.

Discussion of Results.

Water and Solids.—Judging from the fact that the posterior lobe has 2.4% less solids than the anterior, it is physiologically the more active and younger.[1] The water content of the hypophysis is about half way between that of white and gray matter of the brain. It is about 8% higher than that for either muscle or liver and very much higher than for the supporting tissues. It resembles other secretory glands most closely in water content as well as in many other respects.

Proteins.—The fresh anterior lobe consists of 4% more proteins than the posterior lobe. Both lobes contain considerably more than do white or gray matter of the brain, more than muscle, but about the same as liver. The spleen and thyroid contain amounts of protein similar to the hypophysis.

If it is permissible to judge of the amount of nucleoprotein in the hypophysis by the phosphorus present in the protein fraction, it would seem that the percentage of total protein found as nucleoprotein is about the same in the two lobes. It is safe to say that there is about 3 times as much nucleoprotein in the pituitary as in any of the divisions of the nervous system, many times more than in muscle, but probably less than in liver and spleen.

In comparing the distribution of the protein nitrogen in the two lobes, the most apparent fact is the similarity between them. Humin, ammonia, basic, and the monoamino forms are about equally distributed in the two lobes. However, the larger amount of histidin and the smaller amount of cystin in the anterior lobe are probably significant differences. Though the proteins of the lobes of the pituitary have not been isolated and investigated separately, the data above would indicate that the proteins of the two lobes are qualitatively very similar.

Lipins.—It will be noticed that the total lipins are 0 84% higher in the posterior lobe than in the anterior, reversing the protein percentages in the two lobes. Though the white matter of the nervous system has 5

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[1] F. Fenger, "Composition and Physiological Activity of the Pituitary Body," *J. Biol. Chem.*, 25, 417 (1916).

TABLE I.

Constituents in Percentages of Fresh Tissue and of Total Solids.

	Anterior lobe.		Posterior lobe.	
	Fresh tissue.	Total solids.	Fresh tissue.	Total solids.
Water	77.23		79.68	
Solids	22.77		20.32	
Proteins	17.66	77.53	13.46	66.22
Protein phosphorus	0.116	0.509	0.097	0.477
Protein sulfur	0.178	0.782	0.205	1.01
Protein calcium	0.017	0.074	0.032	0.157
Protein nitrogen	2.390	10.49	1.68	8.27
Protein humin nitrogen	0.487	2.15	0.256	1.26
Protein ammonia nitrogen	0.117	0.51	0.073	0.359
Protein basic nitrogen	0.653	2.87	0.513	2.52
Protein arginin nitrogen	0.373	1.64	0.321	1.59
Protein histidin nitrogen	0.104	0.462	0.027	0.132
Protein lysin nitrogen	0.148	0.651	0.075	0.367
Protein cystin nitrogen	0.078	0.34	0.090	0.443
Protein monoamino nitrogen	1.133	4.97	0.841	4.14
Protein non-amino nitrogen	0.285	1.25	0.190	0.935
Protein α-amino nitrogen	0.848	3.73	0.651	3.20
Lipins	3.16	13.87	4.00	19.68
Lipin phosphorus	0.095	0.418	0.12	0.59
Lipin sulfur	0.0012	0.0053	0.0016	0.0079
Cholesterol	0.375	1.65	0.430	2.12
Iodine absorbed	1.94	8.52	2.63	12.94
Lipin residue	2.02	8.87	2.58	12.69
Lipin nitrogen	0.054	0.237	0.077	0.379
Lipin residue nitrogen	0.011	0.048	0.013	0.064
Lipin filtrate nitrogen	0.043	0.189	0.064	0.315
Lipin amino nitrogen	0.025	0.110	0.037	0.181
Lipin choline nitrogen	0.016	0.070	0.021	0.103
Lipin sugar	0.13	0.57	0.15	0.74
Extractives	1.95	8.56	2.87	14.12
Organic extractives	1.56	6.85	2.44	12.00
Inorganic extractives	0.39	1.71	0.43	2.12
Extractive, sulfur	0.003	0.013	0.005	0.025
Extractive, calcium	0.002	0.009	0.008	0.039
Extractive, phosphorus	0.056	0.246	0.068	0.335
Extractive (phosphate) phosphorus	0.036	0.158	0.028	0.138
Extractive neutral phosphorus	0.020	0.088	0.040	0.197
Extractive sugar	0.342	1.50	0.225	1.107
Extractive nitrogen	0.085	0.374	0.168	0.827
Extractive amino nitrogen	0.053	0.233	0.093	0.458
Extractive ammonia nitrogen	0.003	0.013	0.002	0.010
Extractive urea nitrogen	0.007	0.031	0.004	0.020
Extractive creatin + creatinin nitrogen	0.012	0.053	0.009	0.044

TABLE II.

Percentage of Lipins in Fresh Tissue.

	Anterior lobe.	Posterior lobe.
Total lipins	3.16	4.00
Cholesterol	0.375	0.430
Phosphatids	2.45	3.09
Cephalin	1.47	2.16
Lecithin	0.84	1.11
Cerebrosides	0.596 (sugar) 0.55 (res. nitrogen)	0.688 (sugar) 0.65 (res. nitrogen)
Sulfatids	0.06	0.08

TABLE III.

Distribution of Nitrogen, Phosphorus and Sulfur

	Anterior lobe			Posterior lobe		
	% total nitrogen	% total phosphorus	% total sulfur	% total nitrogen	% total phosphorus	% total sulfur
Protein	94.5	43.4	97.7	87.3	34.0	96.9
Lipin	2.13	35.6	0.7	4.0	42.1	0.8
Extractive	3.36	21.0	1.6	8.7	23.9	2.4

times as much lipins as the posterior lobe (20% as against 4%), the gray matter has about the same percentage amount as the pituitary. The percentage of total solids present as lipins is similar to, but less than that in the nervous system, before medullation has occurred. There is considerable similarity between fetal brain and adult pituitary in the percentage of total solids present as lipins and as proteins. Muscle has about $^{1}/_{4}$ as much lipins, most of the glandular tissues have less.[1] The liver, however, contains nearly as much; the thyroid somewhat more.

About the same portion of the total lipins in the two lobes is in the form of *cholesterol*. Both lobes contain less cholesterol than any part of the brain, less even than in very young fetal brains, but contain more cholesterol than do other organs.

The **phosphatids** are calculated from the lipin phosphorus on the assumption that the phosphatids contain 3.88% of phosphorus. This group is about equally distributed between the two lobes. The phosphatids are probably present in amounts about equal to those in gray matter of brain, somewhat greater than in liver, much greater than in muscle, and similar to that in thyroid and spleen.

In the table the lipin amino nitrogen is calculated to *theoretical cephalin*, assuming that it has 1.7% amino nitrogen. However, it is probable that there are small amounts of other lipins that contain amino nitrogen. Cephalin is thus the principal lipin in both lobes of the pituitary, as it is in all divisions of the brain.

Theoretical lecithin is calculated from the choline nitrogen, assuming that 1.9% (all) its nitrogen is in this form. There is about $^{3}/_{5}$ as much lecithin as cephalin in each lobe. These proportions are similar to those in the brain.

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[1] F. Fenger, "Phosphatids in the Ductless Glands," *J. Biol. Chem.*, 27, 303 (1916).

Some nitrogen in filtrate is not amino or choline nitrogen. This may be one of the constituents of tethelin, or possibly of some phosphatids. This may be concerned in the formation of the active principle of the posterior lobe.

The *cerebrosides* can be calculated from the residue nitrogen (cerebrosides = 2.00% N). By this estimation the posterior lobe has 0.65% and the anterior lobe 0.55% cerebrosides. It is probably more accurate to calculate from the sugar formed on hydrolysis assuming that the cerebrosides contain 21.8% sugar. In this way the cerebrosides equal 0.69% in the posterior lobe and 0.60% in the anterior. This is remarkably similar to the amounts found in gray matter, about $^1/_{10}$ that of white matter, but much greater than in most tissues. Pus cells have about the same quantity as the pituitary. The glands of internal secretion may contain large amounts of cerebrosides; the data are meager.

The amount of *sulfatids* is very small, much smaller than in the fetal nervous system. In this respect it is similar to the non-nervous parts of the organism.

Extractives.—If the amount of extractives is a measure of the activity of a tissue, both lobes are among the more active tissues. The posterior lobe has considerably more extractives than the anterior. The posterior has about as much as young nervous tissue, and more than adult nervous tissue. The anterior lobe has approximately the same amount as the muscles, though the amounts of the various forms of extractives differ greatly.

The amount of *inorganic material* in the two lobes differs but slightly, while the amount of *organic material* is almost 1% higher in the posterior. One would expect the secreting portion to be higher in all extractives unless some special material of organic nature is being elaborated. In both lobes the amount of the inorganic extractives is considerably less than in the brain or muscles and most other organs.

There is more *sulfur* and more *calcium* in the posterior lobe. The *phosphorus* as *phosphate* is higher in the anterior lobe, but the *neutral phosphorus* is considerably greater in the posterior. The amount of sugar or other reducing substances in the anterior lobe is greater. The amount of nitrogen is about twice as high in the posterior lobe. The amount of nitrogen in the form of *urea*, *ammonia*, *creatin* and *creatinin* is slightly greater in the anterior lobe.

Probably the most significant data on extractives is the comparatively large amount of nitrogen in the posterior lobe as *amino nitrogen* and *undetermined nitrogen*. These are the two forms that are probably present in the pressor principle of the hypophysis.

It is evident from Table III that the distribution of nitrogen, phosphorus and sulfur is very much the same in the two lobes.

Conclusions and Summary.

1. A method of tissue analysis using small quantities is described. Two to 10 g. of tissue is used for complete analysis. The compounds are separated into 3 groups, proteins, lipins, and extractives. Many determinations are made on aliquot parts of each of these groups.

2. The anterior lobe has 2 4% more solids, 4% more protein, 0.9% less lipins, and 0.9% less extractives than the posterior lobe.

3. The distribution of the various elements and compounds in the protein fraction indicates a close similarity in the nature of the proteins of the two lobes.

4. Except for the small amount of sulfatids in the hypophysis the distribution and amounts of the various lipins are similar to those of gray matter of the cortex. Because of lack of quantitative data it cannot be stated whether the particular pituitary lipins do or do not closely resemble those of the other glands of internal secretion (thyroid in particular).

5. The extractives decidedly predominate in the posterior lobes. In attempting to see in what substances this predominance consists, non-phosphate phosphorus, amino nitrogen and undetermined nitrogen are found to be conspicuous. The two latter may be present in the pressor compound.

6. The chemical composition of the hypophysis resembles the gray matter of the brain or young nervous tissue in most respects. There are many points of resemblance to the thyroid and spleen, quite a few to the liver, but practically none to the connective tissues, muscle, or white matter of the brain. There is no part of this data that would indicate that the pituitary could not have a vicarious relationship to the thyroid.

7. In those respects in which the two lobes differ, the posterior is more like gray brain substance than the anterior. Both lobes resemble each other more closely than either resembles any other tissue. It cannot be stated that the pituitary is more like unmedullated nervous tissue than it is like undifferentiated pus cells. It can be assumed as an hypothesis that the partly differentiated embryological material, after union of the two parts, develops together, resulting in a similarity of composition.

SAN FRANCISCO, CALIFORNIA

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE WORCESTER POLYTECHNIC INSTITUTE.]

THE PREPARATION OF CYANOGEN CHLORIDE.[1]

BY W. L. JENNINGS AND W. B. SCOTT.

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Berthollet,[2] in 1787, was the first to prepare cyanogen chloride by the action of chlorine on hydrocyanic acid. Because of his misconception of the nature of chlorine he called the product "oxidized prussic acid," but did not determine its constitution. In 1815 Gay-Lussac[3] determined its chemical nature, assigned the formula which is accepted to-day, and named it "chlorocyanic acid." His method was to saturate an aqueous solution of hydrocyanic acid with chlorine and remove the excess chlorine by shaking with mercury. The product was at first obtained from the solution by distillation, but as it was thought this heating decomposed it, in later experiments it was separated by reducing the pressure in the flask until the "chlorocyanic acid" was vaporized. Gay-Lussac found later that he could prepare the substance by the interaction of moist hydrocyanic acid and chlorine and by the action of chlorine on dry mercuric cyanide in the sunlight, but he preferred the first method. He did not purify his product well enough to make an accurate determination of its physical constants. From its behavior he concluded that while at ordinary temperature and pressure it appeared to be a gas, this property might be due to the presence of some other gas such as carbon dioxide. Serullas,[4] in 1827, found that the presence of moisture greatly facilitated the reaction between the chlorine and mercuric cyanide; enough water was added to the mercuric cyanide to moisten but not dissolve it. Chlorine was passed into the flask containing the cyanide until most of the air was expelled and the flask was then set aside for from 10 to 12 hours, as it was found that under these conditions direct sunlight was detrimental to the reaction. The product contained hydrochloric acid, cyanogen and chlorine. He found the melting point to be —18 to —20° and the boiling point —12° to —15°, but the product was obviously far from pure. He was the first to name it cyanide of chlorine.

Serullas found that while dry cyanogen and chlorine did not react even in the sunlight, the presence of a little moisture resulted in the formation of a yellow liquid. He also found that pure hydrocyanic acid and moist chlorine, when the latter was not in excess, reacted in the sunlight to give ammonium chloride and the yellow liquid. The yellow liquid had a sharp and irritating odor, was insoluble in water, but soluble in alcohol.

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[1] Published by permission of the Director of the Chemical Warfare Service.

[2] *Ann. chim. phys.*, [1] 1, 35 (1789).

[3] *Ibid.*, [1] 95, 200 (1815).

[4] *Ibid.*, [2] 35, 291, 337 (1827).

Water slowly decomposed it, giving hydrochloric acid, nitrogen, carbon dioxide and a white crystalline solid which he concluded was a chloride of carbon, since it gave chlorine and carbon on decomposition. From these facts he concluded that the yellow liquid was a mixture of nitrogen chloride and carbon tetrachloride formed by the action of chlorine on cyanogen chloride in the sunlight and attributed the unusual stability of the nitrogen chloride (which did not explode) to the presence of the carbon tetrachloride.

In 1847 Wurtz[1] treated a dilute solution of hydrocyanic acid cooled to 0° with chlorine. After some time a liquid layer formed on the surface of the solution. This layer, after separation and washing with water, boiled at 20° and its vapors burned with a violet flame. He called this liquid "chlorohydrure de cyanogene" and gave it the formula $2CNCl.HCN$. When cooled and treated with mercuric oxide to remove the hydrocyanic acid, it decomposed, giving cyanogen chloride, which could be distilled through calcium chloride. When this product contained any excess hydrocyanic acid and chlorine it polymerized to cyanuryl chloride but would not change if entirely pure.

Wurtz determined the boiling point to be 16° and the melting point —7° and considered it a liquid isomer of the gaseous cyanogen chloride. In a later investigation[2] he found the boiling point to be 15.5° and melting point —5° to —6°. These later observations were confirmed by Salet[3] in 1865.

An investigation carried out by Naumann and Vogt[4] in 1870 showed that the product first formed when chlorine was passed into the solutions of hydrocyanic acid was not a compound of cyanogen chloride and hydrocyanic acid, but simply a mixture of these two substances of no fixed proportions.

In 1850 Wöhler[5] prepared cyanogen chloride by adding a slight excess of mercuric cyanide to a saturated solution of this salt in water, and passing in chlorine until the solution was saturated and the space above the liquid was filled with the gas. The flask was then closed, placed in a dark room, and shaken frequently until all the cyanide had dissolved or all the chlorine had been used up. Any excess of chlorine was removed by mercury. The cyanogen chloride was then distilled off through calcium chloride and condensed in a U-tube surrounded by a freezing mixture.

In 1854, Cahours and Cloez[6] described a method which differed from

[1] *Compt. rend.*, 24, 436 (1847); *Ann.*, 64, 307 (1847).

[2] *Jahresber.*, 1851, 379.

[3] *Compt. rend.*, 60, 535 (1865).

[4] *Ann.*, 155, 170 (1870).

[5] *Ibid.*, 73, 220 (1850).

[6] *Compt. rend.*, 38, 354 (1854); *Ann.*, 90, 97 (1854).

the Wöhler method in that a dilute solution of mercuric cyanide was used (100 g. in 4 liters of water) and the chlorine was removed from the product by passing the gas through a tube containing copper turnings.

Langlois,[1] in 1861, used alkaline cyanides in place of mercuric cyanide but found that the action of chlorine evolved so much heat that the temperature rose to 85° or 90°, forming ammoniacal vapors and a black substance. However, by cooling the cyanide solution with ice only a slight brown coloration appeared. The greater part of the cyanogen chloride distilled off at the temperature of melting ice, but some remained behind, forming, according to the author, a compound with the potassium chloride. By heating in a water-bath at 45° to 50° this compound was broken down and the cyanogen chloride was distilled off through a tube containing calcium chloride and copper turnings and condensed in a freezing mixture.

In 1866 Gautier[2] described a method for preparing each of the supposed 3 forms of cyanogen chloride (gaseous, liquid and solid). He attempted to explain the fact that the gaseous cyanogen chloride of Serullas and the liquid form of Wurtz had the same formula by assuming the former was only the vapor of the latter. It is interesting to note that this crude explanation found its way into one of the text-books on chemistry.[3] It was characteristic of all 3 methods that the chlorine was added to the cyanide. In 1895, Hantzsch and Mai[4] reversed this procedure. To a saturated solution of chlorine in water at 0°, potassium cyanide was added until the chlorine was completely used. The solution was then resaturated with chlorine and the addition of potassium cyanide continued. By always keeping the chlorine in excess the authors claimed to have overcome the tendency of the reaction mixture to turn brown, which always happens when chlorine is passed through a solution of potassium cyanide, with consequent low yield of cyanogen chloride.

The most recent method of preparation was that of A. Held.[5] The author claimed that the addition of zinc sulfate to a solution of potassium cyanide made the solution more stable under the action of chlorine. Chlorine was passed into a solution of 4 moles of potassium cyanide and $^{1}/_{2}$ mole of crystalline zinc sulfate in 8 liters of water cooled to 0°, until the cyanide was used up and the white zinc cyanide appeared and then just disappeared. The cyanogen chloride was not distilled from the solution, but a 100% yield was calculated from the quantity of sodium which the cyanogen chloride replaced in an organic molecule to which the sodium was united, such as sodium acetoacetic ester.

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[1] *Ann. chim. phys.*, [3] 61, 481 (1861); *Jahresber.*, 1861, 345.

[2] *Bull. soc. chim.*, 5, 403 (1866); *Ann.*, 141, 122 (1867).

[3] Roscoe and Schorlemmer, 1, 668 (1878 edition).

[4] *Ber.*, 28, 2471 (1895).

[5] *Bull. soc. chim.*, [3] 17, 287 (1897).

Grignard[1] claimed that the method of Held will yield only 25% of the theory and recommended the method of Dreschsel,[2] which is a modification of the Wöhler method. In this method chlorine was passed into a flask $^1/_3$ to $^2/_3$ full of water, cooled in ice-water, until a thick mush of chlorine hydrate was formed. The amount of chlorine added was determined by weighing the flask and contents before and after the addition. Twice this weight of mercuric cyanide was added, the flask closed, and shaken in the dark until all the cyanide was dissolved and the solution was colorless. The cyanogen chloride formed was obtained by distillation. Grignard modified the above procedure by adding an amount of sodium chloride equal to the weight of chlorine to prevent the formation of a chlorocyanide. The time of the operation was about 24 hours.

Experimental.

The first method investigated was that of A. Held,[3] but the yields, after several trials, were so small that it was not thought desirable to purify the product. The next method tried was that of Langlois.[3] The product was purer than that obtained in the method of Held, but the yield was even less, so this method also was abandoned.

As the presence of water seemed to have a marked influence in causing the blackening it was decided to try the action of chlorine on powdered cyanide without the addition of water.

Solid Cyanide with Sand Diluent.—Fifty g. of finely ground potassium cyanide (Baker & Adamson) mixed with an equal bulk of mediumly fine sand, to serve as a heat-distributing medium, were put in a glass tube of 3 cm. diameter. This tube was about 40 cm. long and surrounded by a bath at a temperature of —5°. Chlorine, washed with water, was introduced at the bottom of the tube, and the gas issued at the top through a tube containing copper turnings and calcium chloride and was condensed in a U-tube, cooled to —18° to —19°.

During the run the cyanide in a portion of the tube which was visibly moist turned a dark brown, but that which was seemingly dry did not change color. No product distilled over until the bath surrounding the sand-cyanide mixture had reached a temperature of about +2° or +3°. The final temperature of the bath, 2.5 hours after starting, was +9°. 28 g. of a yellow colored liquid was obtained, which is equivalent to a yield of 50%. A repetition of this experiment under exactly the same conditions except that the surrounding bath was not allowed to rise above +3° gave an 80% yield. Subsequent experiments under apparently the same conditions, gave variable results, in two cases the yields being 88% and 93%, respectively, and in others as low as 10%.

[1] *Ann. chim.*, [9] 4, 40 (1915).

[2] *J. prakt. Chem.*, [2] 8, 328 (1874).

[3] *Loc. cit.*

It seemed probable that variations in moisture and temperature influenced the yield. Experiments were made to determine the effects of a maximum and a minimum amount of water. 50 g. of cyanide triturated with an equal weight of water was treated in a 500 cc. flask with a current of chlorine, the contents of the flask being cooled in a bath at —5° and constantly stirred. The mixture turned dark almost at once upon the entrance of chlorine, which was passed through the mixture for two hours when there appeared to be no more liquid collecting in the receiver. The flask was then heated in a bath at 45° to distil over any cyanogen chloride remaining. There was obtained 11.5 g. corresponding to a yield of 20.7% of a yellow product, somewhat turbid from the presence of cyanuryl chloride formed by polymerization. The behavior of the reaction was quite similar to that of the Langlois method and the yield was unsatisfactory.

In the next experiment the cyanide was carefully dried at 120°, finely powdered and mixed with an equal bulk of sand previously dried. This was treated with chlorine, dried by bubbling through sulfuric acid, for two hours, in the same apparatus and under the same conditions as previously described for the sand-cyanide mixture. No product was obtained which proved that some moisture was essential for the success of the reaction. Any excess of moisture, however, speeded up the reaction to such an extent as to cause local heating with consequent decomposition, formation of azulmic substances, and diminished yield. The best results were obtained with about 2% moisture. In all the experiments with the cyanide-sand mixture examination of the solid residue after the reaction showed that there were numerous scattered areas of decomposition, undoubtedly due to local superheating and excess moisture, the sand particles not being able to distribute this heat rapidly enough. The excess temperature in the zone of reaction drove out the moisture from some areas and deposited it in the cooler portions where it accumulated and led to azulmic formation and lessened yield.

It seemed desirable to find a diluent that would dissipate the excessive heat of the reaction as fast as formed. Carbon tetrachloride proved to be the most effective agent for this purpose.

Solid Cyanide with Carbon Tetrachloride Diluent.—The procedure finally adopted was as follows: 50 g. (1 mole) of Merck's sodium cyanide fused in lumps, purity 98–99%, was finely pulverized and one g. (2%) of water was added and thoroughly mixed with the cyanide. This mixture was put in a 250 cc. filter flask together with 75 cc. of carbon tetrachloride, just enough to prevent the mass becoming pasty, and cooled to —5° by an outside bath of ice and salt at —10°. Chlorine, bubbled through water, was run into the mixture as rapidly as possible with constant shaking of the flask so that the temperature of the reacting mass was held between the limits of —5° and 0°, for the most part actually at —3°. The time required for the complete absorption of chlorine under these conditions was about 4.5 hours. The reacting materials assumed a flesh color shortly after the entrance of the chlorine. This color did not change until nearly the end of the chlorine absorption, when it became slightly darker, due to small amounts of the material spattering up out of the cooled zone and thereby undergoing decomposition. The reaction flask was connected by a calcium chloride drying tube filled with fused calcium chloride to a U-tube immersed in a freezing mixture. The receiver was connected to a water bubbler through another chloride of calcium drying tube. When the chlorine absorption was complete, indicated by gas passing through the bubbler on the end of the absorption tube, the temperature in the reacting flask was allowed to rise to about +10°, at which point the cyanogen chloride began to distil. The distillation was continued with gradual rise of temperature and was completed by surrounding the flask with a warm bath. The heating was discontinued when the temperature inside the flask reached 28°. During the distillation a slow current of chlorine was passed through the apparatus. The cyanogen chloride obtained was slightly yellow in color and weighed 60 g., corresponding to a yield of 98% based on 49 g. of pure sodium cyanide.

The carbon tetrachloride used as a diluent was distilled off on the steam bath and measured 77 cc. It was colored slightly yellow and was somewhat turbid from the small amount of water that distilled over with it. This amount was practically quantitative for the carbon tetrachloride and water originally added. It had a strong odor of cyanogen chloride and upon standing some time deposited a small amount of cyanuryl chloride. The residue of sodium chloride, left after the removal of the carbon tetrachloride, was an almost white powder and had the appearance of the original powdered cyanide. It weighed 60.5 g., showing that all the sodium cyanide had been transformed into sodium chloride. Its aqueous solution gave a slightly alkaline reaction and only a faint test for cyanide. These results show that the reaction was practically quantitative. An experiment run at a somewhat higher temperature (+5°) did not give as satisfactory a yield.

One experiment showed that the process can be carried on without any diluent provided the temperature is kept low enough and the chlorine is supplied only as fast as required. The method used was to expose the finely pulverized sodium cyanide containing 2% moisture in a closed chamber surrounded by a refrigerating atmosphere at a temperature of —18°. The chamber was connected with a reservoir of chlorine under pressure. After 16 hours of contact the cyanide had taken on the appearance of brown sugar and the reaction appeared to be complete. The cyanogen chloride formed was distilled off in the usual manner, giving a yield of 85%. The smaller yield and greater amount of decomposition which was apparent, showed that this method does not permit of such perfect control as when carbon tetrachloride is used as a diluent. The cyanogen chloride may be freed from any dissolved chlorine by solidifying it and sweeping out the chlorine by a slow current of dry air or by letting it stand in a sealed tube over mercury and subsequent distillation. Thus purified, it formed a colorless liquid boiling at 13° at 748 mm. pressure (thermometer bulb immersed in the liquid) and solidifying at —5° to —6°. Regnault[1] gave the boiling point as +12.66° and the melting point as —7.4°. Two vapor-density determinations by the Victor Meyer method gave a molecular weight of 63.6 and 63.8, results which were only slightly higher than the theoretical (61.5).

When pure the cyanogen chloride does not polymerize; the impure products, however, show a varying degree of polymerization, depending upon the conditions. This is especially marked in the presence of small amounts of hydrochloric acid, traces of which are apt to be formed by the action of the chlorine on organic impurities accidentally present. Whenever such traces of hydrochloric acid are suspected they should be removed by lime or other alkaline agent, as they very rapidly polymerize the cyanogen chloride to cyanuryl chloride as explained by Chattaway and Wadmore[2] In the literature[3] the statement is made that great care must be exercised when preparing cyanogen chloride as explosions frequently occur. This idea seems to have originated from a brief note of Weith,[4] who stated that he had often observed explosions of extreme violence when passing chlorine into solutions of mercuric cyanide, he had never observed them, however, when preparing cyanogen chloride by the action of chlorine on hydrocyanic acid. In this connection attention should again be called to the statement of Serullas already referred to in the introduction, that by the action of moist chlorine on an excess of pure hydrocyanic acid in the sunlight he had obtained ammonium chloride and a yellow liquid, which behaved towards water in such a way as to lead him to conclude the yellow liquid was a mixture of nitrogen chloride and carbon tetrachloride, although the nitrogen chloride seemed to be non-explosive.

Because of these statements, it seemed desirable to investigate the cyanogen chloride prepared from solid sodium cyanide as to the possibility of its containing anything of an explosive nature. Ten cc. of a pure sample was cooled nearly to the freezing point and treated with pure dry chlorine. The colorless cyanogen chloride immediately turned yellow and

[1] *Jahresber.*, 1863, 70 and 74

[2] *J. Chem. Soc.* 81, 194 (1902).

[3] Roscoe and Schorlemmer, 1905, Vol 1, 820

[4] *Ber.*, 7, 1745 (1874).

the freezing point was lowered to such an extent that the substance could be cooled to —18° without solidifying. After saturation at —18° the solution was allowed to warm to —10° when boiling began, evidently due to the escape of the excess chlorine. 5 cc. of the material thus saturated with chlorine at —10° was treated with a current of pure anhydrous hydrogen chloride at —5° and allowed to stand in a sealed tube for several days when polymerization to cyanuryl chloride was practically complete except for a few drops of a viscous yellow liquid which resisted further polymerization even upon several week's standing. Considerable pressure was found on opening the tube, owing to the chlorine and hydrogen chloride liberated when the cyanogen chloride solvent was converted to the solid polymer. The few drops of viscous oily liquid were unaffected by a drop of turpentine and there was no evidence of nitrogen chloride or other explosive.

In another experiment, 5 cc. of pure cyanogen chloride saturated at —5° with chlorine was exposed in a sealed tube to direct sunlight for 4 days with apparently no change. The tube, when cooled, and opened showed no pressure. The contents was then saturated with pure dry hydrogen chloride as above. Polymerization appeared to be complete after several days. There was slightly more unpolymerized liquid and it was of a less viscous nature than in the first experiment, but there were no evidences of an explosive compound. The fact that it polymerized almost completely removes the possibility of any secondary effect of sunlight.

In a third experiment 5 cc. of pure cyanogen chloride, without previous addition of chlorine, after saturation at —10° with pure dry hydrogen chloride for $^1/_2$ hour, was sealed in a tube. Polymerization began almost immediately and was complete in about a day. In this case no oily liquid was noticeable and there was no formation of a yellow color.

The results of this investigation seem to show that the method of preparing cyanogen chloride by the action of chlorine on solid cyanide at low temperature and in the presence of slight amounts of moisture, not over 2%, is superior to other methods in ease of manipulation, quantitative yields and purity of product. It may also be concluded that in the preparation of cyanogen chloride by this method nothing of an explosive nature is formed. The yellow color of the impure product is due probably to a solution of chlorine in the cyanogen chloride, which greatly lowers the freezing point and the oily liquid formed after polymerizing the unpurified product may be a lower polymer like the cyanuryl chloride.

Credit is due to Dr. Farrington Daniels for his assistance in some portions of the work.

WORCESTER, MASSACHUSETTS.

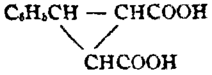
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY.]

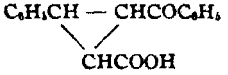
STUDIES IN THE CYCLOPROPANE SERIES. VI.

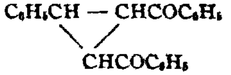
BY E. P. KOHLER AND W. N. JONES.

Received May 17, 1919.

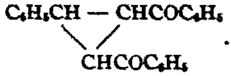
In the last paper of this series[1] the properties of a cyclopropane ketonic acid were compared with those of a closely related cyclopropane diacid. We now present the facts obtained while studying the corresponding diketone. The relation between these substances is shown by the following formulas:



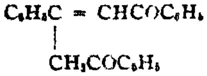




The diketone was obtained by brominating benzylidene diacetophenone and eliminating hydrogen bromide from the product. This reaction might give one of three substances depending on the way in which hydrogen bromide is eliminated: I. A cyclopropane derivative if the hydrogen and bromine come from the α—γ positions

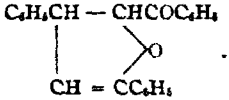


. II. An ethylenic compound if they are removed from adjoining atoms,

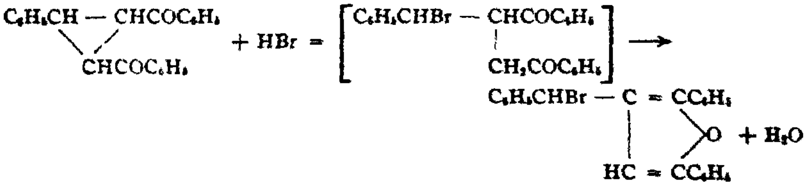


$$\begin{array}{l} C_6H_5C = CHCOC_6H_5 \\ | \\ CH_2COC_6H_5 \end{array}$$

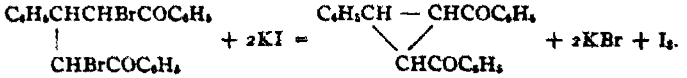
. III. A dihydrofurane derivative if the elimination is from an enolic modification,



. Our substance forms a dioxime, therefore it is not the furane derivative. With hydrogen bromide in glacial acetic acid it gives a bromofurane which has a chain different from that of the ethylenic diketone, and which could be formed only from the cyclopropane derivative



The cyclopropane derivative may also be made by introducing two bromine atoms into benzylidene diacetophenone and digesting the product with potassium iodide.



This method is somewhat more laborious than the former, but admirably shows the ease with which the ring is closed. The product is stereoisomeric with that obtained from the monobromo compound.

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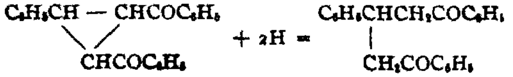
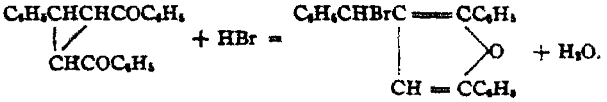
[1] THIS JOURNAL, 41, 1093 (1919).

Phenyldibenzoyl-cyclopropane is a 1,4-diketone as well as a cyclopropane derivative. It gives a dioxime with hydroxylamine and ditertiary alcohols with organic magnesium compounds, but does not show the tendency to form furane derivatives which is characteristic of 1,4-diketones. Its most conspicuous chemical property is that of combining with most of the substances which can be added to α,β unsaturated ketones. With nascent hydrogen, hydrobromic acid, free bromine and phosphorus pentachloride it gives products similar to those obtained from ethylenic compounds. It does not, however, reduce permanganate or give 1,4 addition products with organic magnesium compounds

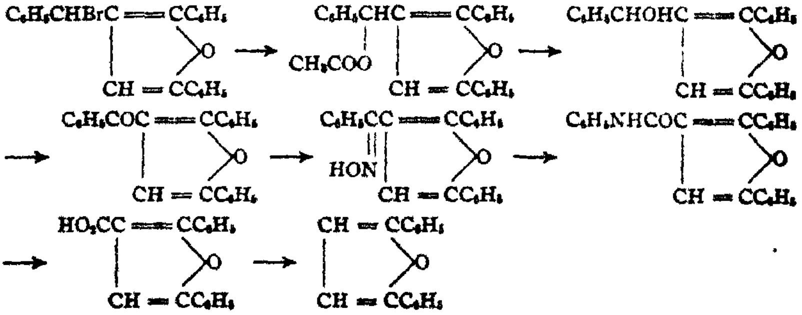
The substance combines with hydrogen more readily than any other cyclopropane derivative that we have studied. Half an hour's boiling with alcohol and zinc dust suffices to reduce it completely to benzylidene diacetophenone, the ring opening at the point at which it had been closed.



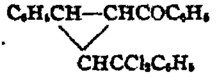
The cyclopropane derivative does not, like the corresponding ketonic acid, combine with halogen acids in alcoholic solution. In glacial acetic acid, however, it combines rapidly with hydrobromic acid. The ring is opened between carbon atoms 2 and 3, and the addition product immediately loses water, thus forming a furane derivative.

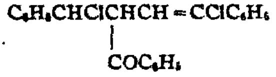


The resulting furane derivative, like most of the addition products obtained in this work, is only remotely related to known substances, hence a number of transformations were necessary to determine its structure. This was finally established by relating it to 1,5-diphenyl furane. The successive steps are shown by the following formulas:

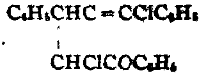


The cyclopropane derivative acts smoothly with phosphorus pentachloride under the conditions that have been found most favorable for the corresponding reaction with unsaturated ketones The products to be anticipated are represented by the following formulas, of which the first represents the compound that would be expected if the ring is not involved, and the others the substances that might be formed by a reaction like that which Straus[1] obtained with benzal-acetophenone.

(I).


(II).


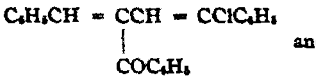
$$\begin{array}{l} C_6H_5CHClCHCH = CClC_6H_5 \\ \qquad\qquad\quad | \\ \qquad\qquad COC_6H_5 \end{array}$$

(III).


$$\begin{array}{l} C_6H_5CHC = CClC_6H_5 \\ \qquad\qquad | \\ \qquad CHClCOC_6H_5 \end{array}$$

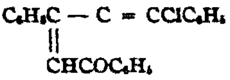
Only one product was obtained. For this the first formula could be discarded at once, for the substance has nothing in common with keto-chlorides of this type; it is not affected by water nor by prolonged boiling with alcohol.

Each of the remaining formulas represents a dichloro compound, containing one active, and one inactive chlorine. In agreement with this the substance readily loses one molecule of hydrogen chloride when boiled with excess of potassium acetate. The possible formulas for the new substances are,

(IV).


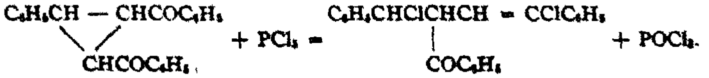
$$\begin{array}{l} C_6H_5CH = CCH = CClC_6H_5 \\ \qquad\qquad\quad | \\ \qquad\qquad COC_6H_5 \end{array}$$

and

(V).


$$\begin{array}{l} C_6H_5C - C = CClC_6H_5 \\ \qquad\qquad \| \\ \qquad CHCOC_6H_5 \end{array}$$

It is not at all easy to distinguish between these two formulas. Each of them represents an α,β-unsaturated ketone, a halogen compound with an unreactive halogen, and a butadiene derivative which on oxidation with permanganate would in all probability give only potassium benzoate and potassium chloride. As the most promising way out of the difficulty we decided to treat the substance with phenyl magnesium bromide. A reaction between an unsaturated ketone such as is represented by Formula IV, and any organic magnesium compound should consist in 1,4 addition to the conjugated system, the final product being a more saturated ketone. The ketone represented by Formula V, on the other hand should give a tertiary alcohol because the two substituents in the β position hinder 1,4 addition to the conjugated system. The substance in question gave an excellent yield of ketone. The cyclopropane derivative therefore reacts with phosphorus pentachloride exactly like an α,β unsaturated ketone, the ring taking the place of an ethylene linkage.



The product obtained by adding bromine to the cyclopropane derivative presented the most difficult problem of all and we have not as yet found a completely satisfactory solution. The only possible formulas are:

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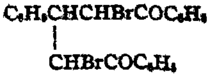
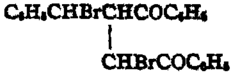
[1] *Ann.*, 394, 290 (1912).

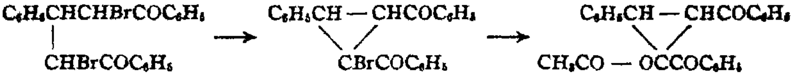


$$C_6H_5CHCHBrCOC_6H_5 - CHBrCOC_6H_5$$



$$C_6H_5CHBrCHCOC_6H_5 - CHBrCOC_6H_5$$

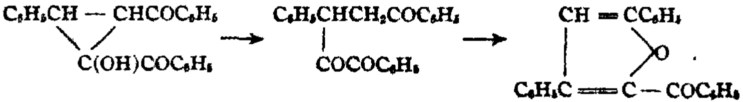
The first represents the dibromo compound used in one of the methods of preparation of the cyclopropane derivative. With potassium acetate it gives either a bromocyclopropane derivative or the corresponding acetate, depending upon the amount of acetate used.



The new dibromo compound gives the same cyclopropane derivative with potassium iodide or zinc, and as it also gives the same products with potassium acetate the two substances therefore may be stereoisomers. On the other hand a substance such as is represented by Formula II could very well give the same products, and as we never obtained both substances in the same reaction, nor were able to transform either into the other, stereoisomerism seems improbable.

The bromo compound obtained by the action of potassium acetate on the dibromide is one of the very few known cyclopropane derivatives which have bromine in combination with a carbon atom of the ring. All efforts to remove another molecule of hydrogen bromide and thus get a cyclopropene derivative were unsuccessful. The bromine is easily replaceable, but it is not possible to get the corresponding hydroxyl compound either by hydrolysis of the bromine derivative with bases or the corresponding acetate with acids.

Evidently the hydroxyl compound rapidly undergoes a rearrangement similar to that which has balked all previous attempts to get hydroxy cyclopropanes. With alkalies the bromo compound gave only yellow oils, which appeared to be diketones, while hydrolysis of the acetate with alcoholic hydrochloric acid gave a furane derivative.



Experimental Part.

The benzal-diacetophenone with which we started was made according to the directions given by Kostanecki.[1] The average yield of pure product was 50%. The diketone reacts with bromine a little above the ordinary temperature, giving either a monobromo or a dibromo substitution product. The result depends largely upon the amount of bromine used; but both of the bromine compounds are sensitive substances which in contact with solutions containing hydrobromic acid change into uncrystallizable gums that materially decrease the yield.

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[1] *Ber.*, 29, 1493 (1894).

α,γ,ϵ-Triphenyl-β-bromo-pentanedione-α,ϵ, : $C_6H_5COCHBrCH(C_6H_5)$-$CH_2COC_6H_5$.—To a warm solution of 50 g. of benzaldiacetophenone in 50 cc. of chloroform, 8.3 cc. of bromine was added while the flask was cooled with tap water. The chloroform was immediately evaporated under reduced pressure, great care being taken to avoid heating the residue. The greenish yellow paste that remained was dissolved in boiling alcohol and deposited a colorless solid, which was purified by recrystallization from the same solvent. The yield of pure product was 46%.

Calc. for $C_{23}H_{19}BrO_2$ Br, 19.6 Found: 19.7.

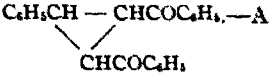
The monobromo compound melts with decomposition at 131°. It is almost insoluble in ether and ligroin, moderately in boiling alcohol and benzene, and very soluble in chloroform.

α,γ,ϵ-Triphenyl-β,δ-dibromo-pentanedione-α,ϵ, $C_6H_5COCHBr(C_6H_5)$-$CHBrCOC_6H_5$.—The dibromo compound was made exactly like the monobromo compound except that twice as much bromine was used with the same amount of ketone. The solvent was allowed to evaporate spontaneously and the residue recrystallized from alcohol.

The yield of pure product was 69%. Since some of this substance is formed whenever the diketone is brominated it was found advantageous to combine the preparation of the mono- and dibromo compounds. For this purpose 8 cc. of bromine was added gradually to a solution of 50 g. of the diketone in 50 cc. of chloroform. The cooled solution was inoculated with the monobromo compound and allowed to stand for several hours, during which time the mono derivative separated. This was filtered off and the filtrate treated with 2 cc. of bromine. The dibromo compound crystallized from the solution. The yield by this method was 47.5 g. of mono- and 12.5 g. of dibromo derivative. The dibromo compound melts with decomposition at 149°. It is very sparingly soluble in ether and ligroin, moderately in boiling alcohol, readily in benzene and chloroform.

Calc. for $C_{23}H_{18}O_2Br_2$: Br, 32.8. Found: 32.9.

1,2-Dibenzoyl-3-phenyl-cyclopropane,



$$C_6H_5CH\overset{\diagdown\;\diagup}{—}CHCOC_6H_5,\ \underset{}{CHCOC_6H_5}$$

.—A number of reagents eliminated hydrogen bromide from the monobromo compound; as all of them gave the same product and since this was insensitive to alkalies, we generally used sodium ethylate. A solution of 1.75 g. of sodium in 50 cc. of alcohol was added to a boiling solution of 25 g. of the monobromo compound in 300 cc. of the same solvent. The reaction went to completion without further heating. The solution deposited 18 g. of crystalline product which gave 15 g. of pure cyclopropane derivative after recrystallization from alcohol—a yield of 75%.

Calc. for $C_{23}H_{18}O_2$: C, 84.6; H, 5.6. Found: C, 84.2; H, 6.0.

The cyclopropane derivative crystallizes in needles and melts at 116°. It is slightly soluble in ether, moderately soluble in boiling alcohol, cold benzene and chloroform. Its solutions in acetone reduce permanganate only on long standing.

An isomeric cyclopropane derivative was obtained by eliminating bromine from the dibromo compound. A solution of three g. each of the dibromo compound and potassium iodide in 150 cc of alcohol was heated on a steam bath for 4 hours. The liquid, which had turned brown after a few minutes' boiling, was then cooled and freed from iodine by shaking with thiosulfate. On evaporation it deposited a yellow solid which became colorless when recrystallized from alcohol. The melting point of the pure compound was 151° The same substance was obtained by boiling an alcoholic solution of the dibromo compound with zinc dust for 25 minutes, but it was impossible to remove all of the bromine without reducing some of the cyclopropane derivative. The yield therefore was small.

Calc. for $C_{23}H_{18}O_2$: C, 84.6; H, 5 6 Found C, 84 2, H, 5 6

The substance is slightly soluble in ether, moderately in boiling alcohol, readily in benzene and chloroform. When recrystallized from alcohol containing 1% sodium hydroxide it passes quantitatively into the isomer which melts at 116°.

The Monoxime.—The two isomeric cylcopropane diketones give the same mono- and dioxime. For preparing the monoxime a solution of 2.7 g. of sodium hydroxide in 5 cc. of water was added to a solution of 5 g. of the cyclopropane derivative and 1.1 g. of hydroxylamine hydrochloride in 100 cc. of alcohol. The mixture was boiled for three hours, then neutralized with hydrochloric acid. On cooling, it deposited white crystals which after one recrystallization from alcohol melted sharply at 144°. The yield was 82%.

Calc. for $C_{23}H_{19}O_2$: C, 80.9; H, 5.6. Found C, 80.7, H, 5 3

The monoxime is sparingly soluble in ligroin and ether, more readily in boiling alcohol, benzene and choroform.

The Di-oxime.—The di-oxime was made like the monoxime but more than twice the amount of hydroxylamine hydrochloride and potassium hydroxide were used for the same quantity of cyclopropane derivative. The product was purified by recrystallization from alcohol. The yield of pure product was 71%.

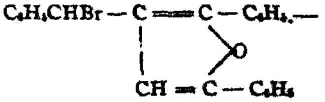
Calc. for $C_{23}H_{20}N_2O_2$: C, 77 5; H, 5.7; N, 7.9. Found· C, 77.9, H, 6 0, N, 7.7.

The di-oxime crystallizes in needles, and melts at 175°. It is sparingly soluble in organic solvents except benzene, chloroform, and boiling alcohol.

Reduction of 1,2-Dibenzoyl-3-phenyl-cylopropane.—In the first experiment the substance was boiled with excess of zinc dust in 80% acetic acid. The sole product was triphenyl-cyclopentane diol, melting at 147°. This result showed that the cyclopropane ring had been opened between the benzoyl groups and a new ring closed, but did not establish the order of these events. The experiment was therefore repeated without the use of acid. A solution of 2 g. of the substance in 60 cc. of 85% alcohol was boiled with excess of zinc dust for an hour. The solution was then filtered and poured into water. This precipitated an oil which soon solidified. After recrystallization from alcohol the solid melted at 85°, and a mixed melting point showed that it was benzal-diacetophenone.

Reaction with Halogen Acids.—In alcoholic solution the cyclopropane derivative is not attacked either by hydrochloric or hydrobromic acid. In glacial acetic acid, hydrobromic acid, in the cold, forms a furane derivative which has bromine in a side chain. Since the cyclopropane derivative is not affected by boiling with glacial acetic acid alone it is evident that the first step consists in addition of hydrobromic acid and that the resulting product, as is usual in the case of 1,4-diketones, subsequently loses water and forms the furane derivative.

2,5-Diphenyl-4-(α-bromobenzyl)-furane,

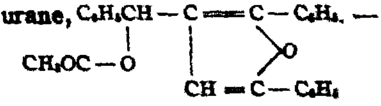


A solution of 5 g. of the cyclopropane derivative in 50 cc. of glacial acetic acid was saturated with hydrogen bromide. The solution gradually turned green, and while standing overnight deposited 5.2 g. of a greenish yellow solid. This was purified by recrystallization from glacial acetic acid.

Calc. for $C_{23}H_{17}OBr$: C, 70.9; H, 4.4; Br, 20.5. Found: C, 70.5; H, 3.9; Br, 20.5.

The bromo compound crystallizes in greenish yellow prisms and melts at 110°. It is sparingly soluble in ether, moderately in ligroin, readily in benzene and chloroform. It is a reactive substance; the halogen is readily replaced by hydroxyl, acetyl, and other groups, and its solution in acetone reduces permanganate at the ordinary temperature.

2,5-Diphenyl-4-(α-acetoxylbenzyl)furane,

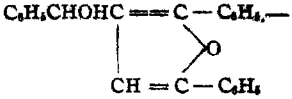


A solution of 3 g. of the bromo compound and 6 g. of potassium acetate in 20 cc. of glacial acetic acid, was heated to near the boiling point for half an hour, then cooled and poured into water. This precipitated a white solid, which after purification from alcohol melted at 84°.

Calc. for $C_{25}H_{20}O_3$: C, 81.5; H, 5.4. Found: C, 82.1; H, 5.5.

The acetate crystallizes in yellow needles. It is moderately soluble in alcohol and in ether, readily in benzene and chloroform. Its solution in acetone reduces permanganate.

2,5-Diphenyl-4-(α-hydroxybenzyl)furane,



The hydroxyl compound was formed both when the bromo compound was hydrolyzed with sodium alcoholate and when the acetate was hydrolyzed with alcoholic hydrochloric acid. A solution of sodium methylate made by dissolving one g. of sodium in 25 cc. of methyl alcohol was added to a hot solution of 5 g. of the bromo compound in 100 cc. of alcohol. The mixture, which was not heated further, gradually deposited 4 g. of the hydroxyl compound, a quantitative yield. A solution of 2 g. of the acetate in 50 cc. of alcohol containing 3% of hydrochloric acid was boiled for 4 hours. On cooling it deposited the same hydroxyl compound which had been obtained in the alkaline hydrolysis.

Calc. for $C_{23}H_{18}O_2$: C, 84 7; H, 5.5. Found: C, 84.4; H, 6 0

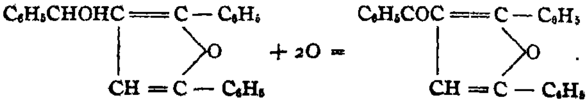
The substance was purified by recrystallization from alcohol. It crystallizes in needles, melts at 105°, and is moderately soluble in ether and boiling alcohol, readily in chloroform. Its solution in acetone reduces permanganate. Boiling glacial acetic acid converts it into the acetate melting at 84°. Oxidation with potassium permanganate gave benzoic acid and oils, but chromic acid in glacial acetic acid resulted in a crystalline product. For the purpose of oxidation 3 g. of chromic anhydride was added to a cold solution of 5 g. of the hydroxyl compound in glacial acetic acid. As the solution warmed up the temperature was controlled by cooling under the tap. The mixture was allowed to stand overnight, then diluted with 100 cc. of water and digested on a steam bath in order to coagulate the oil which was precipitated. The aqueous layer was decanted, the oil washed with water, and dissolved in methyl alcohol. The solution yielded a solid which, after a few recrystallizations from the same solvent, melted at 89°. The yield was 2.4 g.

The analyses of this substance gave variable results until it was discovered that it readily loses water. The loss in weight on drying at 110° was 4.9%. Analyses of the dried material gave the following results:

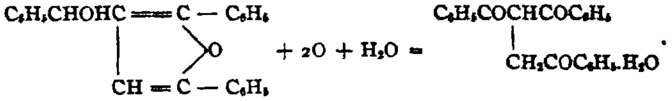
Calc. for $C_{23}H_{18}O_3$ C, 80.7; H, 5.3. Found. C, 80.7; H, 5.5.

Calc. for $C_{23}H_{20}O_4$: H_2O, 5.0; m. w. 360. Found. H_2O, 4.7; m w 340

The substance to be expected in this oxidation is benzoyl-diphenylfurane.

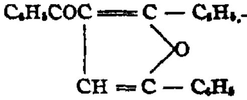


The product actually isolated differs from this by 2 molecules of water. One of these is held very loosely as it is lost when the substance is heated to 110°. The other is removed when the substance is boiled with alcoholic potassium hydroxide, hydrochloric acid in methyl alcohol, or acetic anhydride and sodium acetate. As all of these reagents have the power of transforming 1,4-diketones into furane derivations, it is possible that the furane ring is opened during the oxidation and that the product is a triketone which crystallizes with one molecule of water.



It seems quite as likely, however, that during the process of oxidation the furane derivative combines with two molecules of water and forms a tetrahydro furane derivative. As the purpose of the oxidation was to determine the structure of the hydroxyl compound this matter was not investigated further.

2,5-Diphenyl-4-benzoyl-furane,

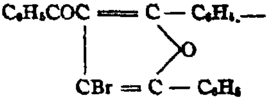


—A solution of 4.5 g. of the oxidation product in 45 cc. of methyl alcohol was boiled with 4 g. of potassium hydroxide for 4 hours. A yellow oil separated during the process and increased in amount when the solution was allowed to stand for some time at the ordinary temperature. This was washed and dissolved in methyl alcohol. The solution gave 1.2 g. of yellow needles. The aqueous layer was carefully examined for sodium benzoate, but none was found.

Calc. for $C_{23}H_{16}O_2$· C, 85.2; H, 5.0. Found: C, 84.8, 84.7; H, 5.0, 5.2.

The same benzoyl derivative was obtained when the oxidation product was boiled with acetic anhydride containing a trace of sodium acetate, and with methyl alcoholic hydrochloric acid. It is moderately soluble in boiling alcohol, readily in ether, benzene and chloroform.

2,5-Diphenyl-3-bromo-4-benzoyl-furane,

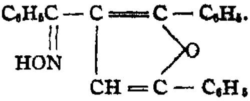


—Diphenyl-benzoyl-furane, in chloroform solution, was treated with a very little more than the calculated amount of bromine. The chloroform, on evaporation, left a pale yellow solid. This, after crystallization from alcohol, melted at 120°.

Calc. for $C_{23}H_{17}O_3$: C, 65.5; H, 4.0. Found: C, 65.7; H, 3.7.

The bromo compound crystallizes in yellow needles. It is moderately soluble in cold alcohol, readily in hot alcohol, ether and chloroform. The bromine is quite unreactive. The substance was boiled in alcoholic solution with potassium acetate for 10 hours, with potassium hydroxide for 4 hours, and with sodium methylate for 3 hours, and in each case recovered unchanged.

The Oxime of 2,5-Diphenyl-4-benzoyl-furane,

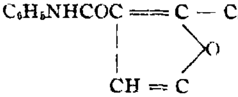


—The oxidation product was boiled with methyl alcoholic potassium hydroxide for 4 hours in order to insure complete conversion into diphenylbenzoyl-furane. Hydroxylamine was then added to the solution and the boiling continued for two hours more. Most of the alcohol was distilled off and the residue poured into water and the solution neutralized with hydrochloric acid. The resulting solid was purified by crystallization from alcohol.

Calc. for $C_{23}H_{17}O_2N$: C, 81.4; H, 5.0 Found. C, 81.8; H, 5.4

The oxime crystallizes in rosets of needles and melts at 174°. It is slightly soluble in ether, moderately in boiling alcohol, readily in benzene and chloroform.

2,5-Diphenyl-furane-carboxanilide,

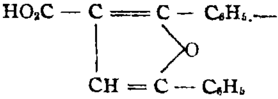


— The oxime readily undergoes the Beckmann re-arrangement to the corresponding anilide. A suspension of 5 g. of the oxime and 7.5 g. of phosphorus pentachloride in dry ether was allowed to stand at the ordinary temperature overnight. The ether was then distilled off and the residue decomposed with ice water. The solid was washed until free from phosphorus compounds, and recrystallized from alcohol.

Calc. for $C_{23}H_{17}O_2N$: C, 81.4; H, 5.0 Found: C, 81.4; H, 5.1

The anilide crystallizes in colorless needles and melts at 187°. It is slightly soluble in ether and alcohol, moderately in hot benzene, readily in chloroform.

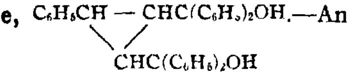
2,5-Diphenyl-furane Carboxylic Acid-4,



—A solution of 4 g. of the anilide and 15 g. of potassium hydroxide in 50 cc. of alcohol was boiled for 10 hours. The alcohol was then distilled off and the residue distilled with steam as long as aniline could be detected in the distillate. This left a solid which was almost completely soluble in 400 cc. of water. After filtration to remove a small quantity of resin, acids precipitated a colorless solid, which was purified by recrystallization from alcohol. It melted at 217°.

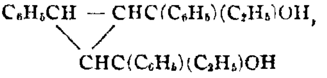
Calc. for $C_{17}H_{12}O_3$. C, 77.3; H, 4.5. Found: C, 77.0; H, 4.6.

The acid has both the composition and the melting point of the 2,5-diphenyl-furane-carboxylic acid-3 described by Paal and Lapf, Perkin, and Thiele. In order to complete its identification it was distilled with zinc dust. The product was 2,5-diphenyl-furane—identified by a mixed melting point, using a specimen on hand.

Reaction with Grignard Reagents, 1,2-Diphenylcarbinyl-3-phenylcyclopropane,  $C_6H_5CH - CHC(C_6H_5)_2OH$, $CHC(C_6H_5)_2OH$.—An ethereal solution of phenyl magnesium bromide was made from 7.59 g. of magnesium in the usual way. The solution was cooled in a freezing mixture, treated with 20 g. of the cyclopropane derivative, which was added in small quantities as a fine powder. The mixture was allowed to stand at the ordinary temperature for several hours, before it was decomposed with iced acid. The ethereal layer, on evaporation, left a solid imbedded in a pasty oil. Recrystallization from alcohol gave a solid, crystallizing in clusters of fine needles melting at 183°. The yield was 42%.

Calc for $C_{35}H_{30}O_2$: C, 87.1, H, 6.3 Found C, 87.3, H, 6.4

The composition of the product shows that it was formed as a result of the combination of one molecule of cyclopropane derivative and two of phenyl magnesium bromide In order to determine whether either of the latter had been taken up in the 1,4 position, giving an open chained ketone, 1.5 g of the substances was added to a large excess of ethyl magnesium bromide There was free evolution of ethane. The resulting magnesium derivative, treated in the usual way, yielded only unchanged substance This, therefore, is not a ketone, but a ditertiary alcohol, showing that the phenyl magnesium bromide had not attacked the ring.

1,2-(α-Phenyl-α-ethyl-carbinyl)-2-phenyl Cyclopropane,  $C_6H_5CH - CHC(C_6H_5)(C_2H_5)OH$, $CHC(C_6H_5)(C_2H_5)OH$ was obtained when the cyclopropane derivative was treated with ethyl magnesium bromide and the product isolated in the usual way. It was purified by recrystallization from ligroin. It melts at 129° and is moderately soluble in ligroin, ether, and alcohol; very soluble in acetone. The yield was 35%.

Calc for $C_{27}H_{30}O_2$ C, 83.9, H, 7.9 Found C, 83.5; H, 7.8

Reaction with Phosphorus Pentachloride, 1,4-Diphenyl-1,4-dichloro-3-benzoyl-butene-4, $C_6H_5CHCl—CH(COC_6H_5)CH = CClC_6H_5$.—A solution of 10 g. of the cyclopropane derivative and 6.4 g. of phosphorus pentachloride in 30 cc. of dry benzene was boiled for 10 hours, cooled and poured on cracked ice. The benzene layer was separated, washed until free from phosphorus compounds, dried, and evaporated under reduced pressure. It left an oil, which was dissolved in alcohol. The alcoholic solution slowly deposited a solid which after two recrystallizations from the same solvent showed a constant melting point of 122°.

Calc. for $C_{23}H_{18}OCl_2$: C, 72.5; H, 4.7; Cl, 18.6. Found: C, 72.3; H, 4.8; Cl, 18.7.

The substance is sparingly soluble in ether, moderately in hot alcohol, readily in benzene and chloroform. It was not affected by boiling with water and it was recovered unchanged after it had been boiled for 10 hours with a 3% solution of hydrochloric acid in methyl alcohol. It is therefore not a ketochloride formed by replacing the oxygen of one of the carbonyl groups with 2 atoms of chlorine.

1,4-Diphenyl-2-benzoyl-4-chloro-butadiene, $C_6H_5CH = C(COC_6H_5)$-$CH = CClC_6H_5$.—A solution of 10 g. of the dichloro compound and 30 g. of anhydrous potassium acetate in 150 cc. of dry methyl alcohol was boiled for 10 hours. Most of the alcohol was distilled off, and the residue diluted with water. This precipitated an oil which soon solidified. The solid was thoroughly washed with water and then recrystallized from alcohol.

Calc. for $C_{23}H_{17}OCl$: C, 80.1; H, 4.9. Found: C, 80.0; H, 5.0.

The substance crystallizes in colorless prisms and melts at 84°. Its solution in acetone reduced permanganate, giving benzoic acid as the only organic product.

1,1,4-Triphenyl-2-benzoyl-4-chloro-butene-3, $(C_6H_5)_2CHCH(COC_6H_5)$-$CH = CClC_6H_5$.—An ethereal solution of phenyl magnesium chloride containing 2 g. of magnesium was prepared in the usual way and cooled in a freezing mixture. To it was added 5 g. of the unsaturated chloroketone in small quantities, and as a finely powdered solid. Each addition produced a yellow color which quickly disappeared again. The mixture was poured into iced acid as soon as all of the substance had been added. The product, isolated in the usual way, and purified by crystallization from alcohol, separated in large, colorless prisms which melted at 140°.

Calc. for $C_{29}H_{23}ClO$: C, 82.4; H, 5.4. Found: C, 82.1; H, 5.7.

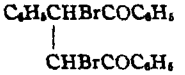
In order to determine the presence or absence of a hydroxyl group, the substance was added to ethyl magnesium bromide. It reacted vigorously, but no evolution of gas accompanied the reaction and no unchanged substance was recovered when the magnesium derivative was acidified. The product is therefore a ketone formed by 1,4-addition, and not a tertiary alcohol such as would be obtained by addition of phenyl magnesium bromide to a carbonyl.

Action of Bromine on the Cyclopropane Derivative.—Bromine reacts with the substance very readily but it is difficult to confine the reaction to the first step. In order to get a crystalline product it was necessary to use small quantities of material. A solution of 2 g. of the substance and 0.33 cc. of bromine in 4 cc. of chloroform was warmed for a few seconds to start the reaction. As soon as the color of the solution had disappeared, 50 cc. of alcohol was added to prevent further change. The product was a mixture, but repeated recrystallization from alcohol resulted in a pure substance which melted with decomposition at 129°.

Calc. for $C_{23}H_{18}O_2Br_2$. Br, 32.9. Found: Br, 32.9.

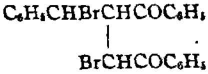
The substance is isomeric with the α,γ-dibromo compound obtained by direct bromination of benzal-acetophenone. With potassium iodide it gave the same cyclopropane derivative that was obtained from the α,γ-dibromo compound, and both substances also gave the same monobromo compound with potassium acetate.

The possible formulas of the addition product are therefore



$$\begin{array}{c}C_6H_5CHBrCOC_6H_5\\ |\\ CHBrCOC_6H_5\end{array}$$

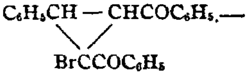
and



$$\begin{array}{c}C_6H_5CHBrCHCOC_6H_5\\ |\\ BrCHCOC_6H_5\end{array}$$

The first formula represents a stereoisomer of the compound, obtained by direct bromination; the second a structural isomer formed by opening the ring between carbon atoms 1 and 2. Both the known α,γ-compound and the substance under consideration first lose hydrogen bromide when treated with any reagent capable of replacing bromine. Since both give the same product when hydrogen bromide is removed, the only method available for distinguishing between them was to transform them into furane derivatives with acid reagents. This was tried with alcoholic hydrogen bromide, and also with acetic anhydride; but both substances gave only oily products.

1,2-Dibenzoyl-2-bromo-3-phenyl-cyclopropane,

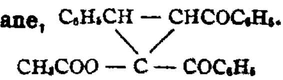


.—A solution of 10 g. of the α,γ-dibromo compound in 200 cc. of absolute alcohol was treated with 2.2 g. of potassium acetate and 5 g. of precipitated calcium carbonate, and the whole boiled for 4 hours. The mixture was then poured into water. This precipitated a solid which was recrystallized from alcohol. The yield was 4 g., or 47%.

Calc. for $C_{23}H_{17}O_2Br$. C, 68.1, H, 4.2, Br, 19.7. Found. C, 68.1; H, 4.4; Br, 19.7.

The substance crystallizes in needles and melts at 122°. It is sparingly soluble in ether and cold alcohol, moderately in boiling alcohol. Our attempts to remove another molecule of hydrogen bromide from this substance and thus get a cyclopropene derivative were unsuccessful. Alkalies gave only oily products and potassium acetate replaced bromine with acetyl.

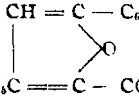
1,2-Dibenzoyl-2-acetoxy-3-phenyl-cyclopropane,



—A solution of 10 g. of dibromo compound in 200 cc. of absolute alcohol was treated with 10 g. of fused potassium acetate and 5 g. of precipitated calcium carbonate. The mixture was boiled for 4 hours, then filtered while hot and allowed to crystallize. The product was purified by recrystallization from alcohol.

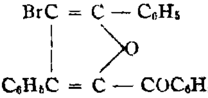
Calc. for $C_{25}H_{20}O_4$: C, 78.1; H, 5.2. Found C, 77.7; H, 5.9.

The substance melts at 159°. Its solution in acetone very slowly reduces permanganate. An attempt to get the corresponding hydroxyl compound failed; alkalies led to unmanageable oils while acids resulted in the formation of a furane derivative.

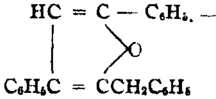
2-Benzoyl-3,5-diphenyl-furane,  .—Twelve cc. of conc. hydrochloric acid was added to a solution of 10 g. of the acetoxy compound in 80 cc. of alcohol. The mixture was boiled for 4 hours. On cooling it deposited a pink colored solid in fine plates. The pink color disappeared on recrystallization from alcohol, which yielded colorless plates melting at 118°.

Calc. for $C_{23}H_{16}O_2$: C, 85.2; H, 5 1, m. w. 324. Found. C, 85 0; H, 4.9; m. w. 329.

The furane derivative is sparingly soluble in alcohol, readily in benzene and chloroform. It has one hydrogen that is replaceable by bromine. With excess of hydroxylamine it forms only a monoxime even on prolonged boiling. It therefore contains but one carbonyl group—proof that it is a furane derivative and not the isomeric cyclopropane. Nascent hydrogen attacks the benzoyl group and reduces it to a benzyl group without either opening or saturating the ring.

2-Benzoyl-4-bromo-3,5-diphenyl-furane,  .—A solution containing 5 g. of the furane derivative and 2.5 g. of bromine was gently warmed until the color disappeared. The solution on evaporation left the bromo compound as a colorless solid which, after recrystallization from alcohol, melted at 110°. The bromine is completely inactive, not a trace of silver bromide being formed on protracted boiling with silver acetate.

Calc. for $C_{23}H_{15}BrO$· C, 68.4; H, 3 7; Br, 19.8. Found C, 68.1; H, 3 9; Br, 19 9.

2-Benzyl-3,5-diphenyl-furane, .—A solution of 4 g. of benzoyl-diphenyl-furane in 50 cc. of glacial acetic acid was heated on a steam bath and treated with 5 g. of zinc dust in small portions. A yellow solid separated during the process and a viscous yellow oil was precipitated when the solution was poured into water. Both the solid and the oil were dissolved in boiling acetone. On addition of alcohol to the hot solution, the product separated in bright yellow needles melting at 193°. The mother liquors contained unchanged substance.

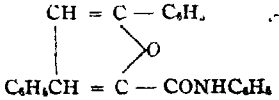
Calc. for $C_{23}H_{18}O$: C, 89.3; H, 5.8. Found: C, 89.3, H, 6.1.

The substance is very sparingly soluble in all solvents except hot acetone and hot chloroform.

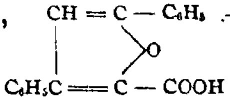
The Oxime of benzoyl-diphenyl-furane was made by boiling an alcoholic solution of 4 g. of the ketone, 4 g. of hydroxylamine hydrochloride, and 5 g. of potassium hydroxide for 4 hours. Most of the alcohol was distilled off and the residue poured into water. The resulting solid, after recrystallization from ethyl alcohol, melted at 152°.

Calc. for $C_{23}H_{17}O_2N$: C, 81.4; H, 5. Found: C, 81.1; H, 5 2.

The oxime crystallizes in needles. It is insoluble in water, moderately soluble in alcohol, readily in ether.

3,5-Diphenyl-furane Carboxanilide-2,  .—For the purpose of rearranging the oxime an ethereal solution of the substance was allowed to stand in contact with excess of phosphorus pentachloride for several hours and then cautiously decomposed with ice water. The resulting oil, after thorough washing with water, was dissolved in alcohol. It separated in colorless needles melting at 143°.

Calc. for $C_{23}H_{17}O_2N$. C, 81.4; H, 5 0. Found: C, 81.1; H, 5.2.

3,5-Diphenyl-furane Carboxylic Acid-2,  .—The anilide was hydrolyzed by prolonged boiling with alcoholic potassium hydroxide, and the resulting acid recrystallized from alcohol.

Calc. for $C_{17}H_{12}O_3$. C, 77.3; H, 4.5. Found· C, 77.7; H, 4.7.

The acid melted with decomposition, at 194°. When heated with zinc dust it gave 3,5-diphenyl-furane which distilled without decomposition, crystallized in irridescent plates, that melted at 109°, gave a blue fluorescent solution in conc. sulfuric acid, and was identical in every way with the α,γ-diphenyl-furane described by Engler and Dengler.[1]

CAMBRIDGE, MASS

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[1] *Ber.*, 26, 1447 (1893).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA.]

ASYMMETRIC DYES.

BY C. W. PORTER AND C. T. HIRST.

Received May 19, 1919

Differential stains are among the most important aids employed in bacteriological and histological work. Although no definite relationship has been established between the chemical structures of dyes and their functions as vital stains, still we considered it a reasonable assumption that selective action in staining might be demonstrated if experiments were made with dyes representing great diversity in structure. In our search for evidence in support of this assumption we have found one racemic mixture upon which wool acts selectively, absorbing more of the levo than of the dextro form of the dye.

The most exhaustive research in this field has been conducted by H. M. Evans,[1] who has reached the conclusion that staining in living tissue with benzidine dyes is a physical rather than a chemical phenomenon. In this opinion Evans is supported by Schulemann[2] and others.

In no instance recorded, however, has an optically active dye been employed as a vital stain. Inasmuch as specificity in enzyme action is closely related to the asymmetric structure of the substrate, it seemed to us worth while to investigate the action of dyes having at least one asymmetric carbon atom in each molecule. We have, therefore, synthesized a group of asymmetric dyes and have made some preliminary experiments on dyeing with them. The results of these experiments, including partial resolution of a racemic dye with concomitant dyeing of wool, give some support to our theory, and the work is being repeated on a quantitative basis. No experiments have yet been made on living tissue.

We desire to present in this paper only a description of the dyes synthesized. The dyes were derived from *p*-amino-benzophenone which was prepared from benzoyl chloride and phthalanilid in the presence of zinc chloride.[3] From this ketone several amino-diphenylalkyl carbinols were prepared by the Grignard reaction. The carbinol carbon was thus rendered asymmetric. *p*-Amino-benzohydrol[4] was prepared also by reducing the ketone in alcoholic solution by means of sodium amalgam. These amines were diazotized and coupled as indicated below.

In preparing the alkyl derivatives of amino-benzophenone it is necessary to use an excess of alkyl magnesium iodide, for the reagent acts quantitatively upon the amino group before the carbonyl group is attacked; and unless both parts of the molecule have been acted upon, the original ketone is regenerated by hydrolysis. The addition products formed between the amino-benzophenone and alkyl magnesium iodide were hydrolyzed by pouring into cold saturated solutions of ammonium chloride. The carbinols were obtained from the ether layer and recrystallized from hot ligroin.

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[1] Evans, *Sci.*, 39, 443 (1914).

[2] Schulemann, *Deut. Med. Woch.*, 40, 1839 (1914).

[3] Dobner, *Ann.*, 210, 260 (1881).

[4] Kippenberg, *Ber.*, 30, 1136 (1897).

p-Amino-diphenylmethyl-carbinol.

The compound was formed by the action of methyl magnesium iodide on *p*-amino-benzophenone. It is a colorless crystalline body melting at 101°. It appears among the reaction products as a red oil and crystallizes only when quite pure. It is soluble in alcohol, chloroform, acetone and in hot ligroin. The ligroin solution on cooling yields the crystals in the pure state.

Calc. for $C_6H_5C(OH)(CH_3)C_6H_4NH_2$ C, 78.87; H, 7.04, N, 6.58. Found· C, 78.80; H, 7.14; N, 6.56.

The corresponding ethyl derivative crystallizes in colorless plates melting at 103°. It dissolves in glacial acetic acid from which it may be precipitated by the addition of water. Crystallization from hot ligroin affords the best means of purification.

Calc. for $C_6H_5C(OH)(C_2H_5)C_6H_4NH_2$. C, 79.25; H, 7.49; N, 6.17. Found: C, 79.00; H, 7.52; N, 6.16.

Diphenyl-methylcarbinol-*p*-azo-β-naphthol.

The amine described above was diazotized and coupled with β-naphthol with the production of a red dye. The compound is soluble in hot alcohol from which it crystallizes on cooling. It is soluble in the ordinary organic solvents and practically insoluble in water, dilute acids and alkalies. It melts at 190°.

Calc. for $C_6H_5C(OH)(CH_3)C_6H_4N = NC_{10}H_6OH$: C, 78.30; H, 5.44; N, 7.61. Found. C, 78.30; H, 5.40; N, 7.65.

Diphenyl-methylcarbinol-*p*-azodimethyl-aniline.

Success in preparing this dye depends largely upon the control of the hydrogen-ion concentration. Dimethyl-aniline hydrochloride was dissolved in 0.1 *N* hydrochloric acid. The primary amine was diazotized in acid of the same concentration to which an equivalent quantity of sodium acetate had been added. The dye has a deep red color in acid solution and is yellow in alkaline solution It may be purified by crystallization from hot alcohol. M. p. 177°.

Calc. for $C_6H_5C(OH)(CH_3)C_6H_4 - N = N - C_6H_4N(CH_3)_2$: C, 76.48; H, 6.72; N, 12.17. Found: C, 76.40; H, 6.65; N, 12.15.

Naphthol sulfonic acid and naphthylamine sulfonic acid derivatives were synthesized for the production of water-soluble dyes. Corresponding compounds were prepared from *p*-amino-diphenyl-ethylcarbinol and from

TABLE I

Properties of Dyes

		M. p.	Color	Water	Acids	Bases	Alcohol
(1)	$C_6H_5CHOHC_6H_4N_2C_{10}H_6OH$	169.5°	red	insol.	insol.	insol.	sol.
(2)	$C_6H_5CCH_3OHC_6H_4N_2C_{10}H_6OH$	190°	red	insol.	insol.	insol.	sol. (hot)
(3)	$C_6H_5CC_2H_5OHC_6H_4N_2C_{10}H_6OH$	149°	crimson	insol.	insol.	insol.	s. sol.
(4)	$C_6H_5CHOHCH_4N_2C_6H_4N(CH_3)_2$	145°	red	sl. sol.	sol.	insol.	sol.
(5)	$C_6H_5CCH_3OHC_6H_4N_2C_6H_4N(CH_3)_2$	177°	yellow	insol.	sol.	sol.	sol. (hot)
(6)	$C_6H_5CC_2H_5OHC_6H_4N_2C_6H_4N(CH_3)_2$	138–9°	orange	sol.	sol.	sol.	sol.
(7)	$C_6H_5CHOHC_6H_4N_2C_{10}H_4OH(SO_3H)_2$	162°	red	insol.	sol.	insol.	sol.
(8)	$C_6H_5CC_2H_5OHC_6H_4N_2C_{10}H_5OHHSO_3$	120.2°	dark red	v. sol.	sol.	sol.	sol.
(9)	$C_6H_5C(CH_3)OHC_6H_4N_2C_{10}H_5OHHSO_3$	150–2°	red	v. sol.	sol.	sol.	sol.

p-amino-benzhydrol. They are very much alike in properties, but vary in color from yellow to crimson.

The first 3 compounds listed in this table constitute examples of alkali-insoluble phenols (naphthols). The insolubility of these dyes lends support to the theory of Torrey and Kipper,[1] *viz.*, that phenols are generally insoluble if in each molecule there is a long side chain *ortho* to the hydroxyl group and at least one other substituent in the ring. In this case the C_4H_4 residue of the naphthalene constitutes the auxiliary substituent. The behavior of these dyes in dilute alkalies is in harmony also with Adams'[2] more recent theory concerning the solubility of phenols.

BERKELEY, CAL.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY.]

THE OXIDATION OF ETHYL ALCOHOL BY MEANS OF POTASSIUM PERMANGANATE.

BY WILLIAM LLOYD EVANS AND JESSE E. DAY.

Received May 22, 1919

A preliminary report of a portion of the work included in this paper has already been made.[3] The influence of the alkali on the oxidation of organic and inorganic compounds by means of potassium permanganate has been studied by other early investigators (Margueritte, Pelouze, Bussey, Hempel and Berthelot) in addition to those mentioned in the preliminary article.

Among the objects of this investigation were the following: (1) to ascertain what are the reaction products when ethyl alcohol is oxidized both in neutral and in alkaline potassium permanganate solutions under known conditions of temperature; (2) to study the effect of temperature, of change in the initial concentration of the alkali present, and their combined effect on the character of the reaction products; (3) to study the mechanism of the oxidation of ethyl alcohol under these variable conditions.[4]

It has been definitely established that acetic acid is the only product obtained when ethyl alcohol is oxidized by an aqueous solution of potassium permanganate, but that acetic acid, oxalic and carbonic acids are also formed when the oxidation is conducted in the presence of potassium hydroxide the concentration being above certain minimum values (p. 1282). Hepter,[5] studying the action of potassium permanganate on organic compounds in acid and alkaline solution, found that substances having an alkyl group were always oxidized by alkaline permanganate to the corresponding aliphatic acid, carbon dioxide and oxalic acid, and the results were dependent upon the temperature of the reaction mixture and upon the position which the intermediate oxidation substance occupied in its own homologous series.

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[1] Torrey and Kipper, THIS JOURNAL, 30, 840 (1908).

[2] Adams, *Ibid.*, 41, 247 (1919)

[3] THIS JOURNAL, 38, 375 (1916).

[4] *Ibid.*, 38, 377 (1916).

[5] *Z. anal. Chem.*, 51, 409–29 (1912).

Barendrecht[1] determined alcohol in rather dilute solution by adding the alcohol to a boiling mixture of potassium permanganate and potassium hydroxide solutions, in which it is oxidized to carbon dioxide: $C_2H_5OH + 12KMnO_4 + 12KOH \longrightarrow 12K_2MnO_4 + 9H_2O + 2CO_2$. He noticed that the temperature was an essential factor in the complete conversion of the alcohol to carbon dioxide.

Cochenhausen,[2] on treating acetone with potassium permanganate in solution with potassium hydroxide found that it was oxidized to acetic, oxalic and carbonic acids. Greifenhagen, Koenig and Scholl[3] estimated carbohydrates, polyhydric alcohols, the corresponding aldehydes, ketones, and polysaccharides by oxidizing them to oxalic and carbonic acid with alkaline potassium permanganate. Greifenhagen found that the formation of oxalic acid and carbon dioxide was quantitative, and was dependent upon the alcohol, aldehyde and ketone groups.

Witzemann[4] has investigated the character of the reaction products obtained by oxidizing acetone with potassium permanganate with varying initial concentrations of alkali. His experimental results were similar to those reported by us in our previous paper.

Experimental Part.

(*a*) **Methods of Analysis.**—The methods of analysis were the same as those described in our first paper, together with the following addenda.

Oxalic Acid.—The acid was first precipitated as the calcium salt by the method previously described for its quantitative determination. The salt was then filtered, washed and finally dissolved in slightly more than its equivalent of dil. sulfuric acid. On the addition of an equal volume of absolute alcohol the calcium sulfate was precipitated and removed. On spontaneous evaporation the free oxalic acid crystallized out in the well defined needle form. This procedure cannot be quantitative because of the presence of the slight excess of sulfuric acid. The purity of the product was checked by a melting-point determination. Another qualitative test for oxalic acid was that contained in our preliminary paper.[5]

An aliquot part of the solution containing the oxidation products was used to determine the oxalic acid present as potassium oxalate. With phenolphthalein as the indicator the sample was first slightly acidulated with 20% acetic acid boiled for a few minutes to drive off carbon dioxide, then made barely alkaline with ammonium hydroxide after which the oxalate was precipitated by 5% calcium acetate solution. The removal of the carbon dioxide was unnecessary but insured the absence of carbonate in the calcium precipitate. After filtering and washing the calcium oxalate on purified asbestos in a Caldwell crucible, it was titrated against standard potassium permanganate solution in the presence of 5% sulfuric acid in the usual manner. The filtration, washing and titration of the insoluble oxalate, when carried out as described, were found to be more rapid and satisfactory than when the precipitate was collected and washed on a filter paper, dissolved by means of sulfuric acid and then titrated.

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[1] *Z. anal. Chem.*, 52, 167–72 (1913).

[2] *J. prakt. Chem.*, [2] 58, 451 (1898).

[3] *Biochem. Z.*, 30, 151 (1910); 35, 169–193 (1911).

[4] THIS JOURNAL, 39, 2657 (1917).

[5] *Ibid.*, 38, 378 (1916).

Acetic Acid.—Methods were examined for the determination of this acid by the use of (1) hydrochloric acid, (2) sulfuric acid, (3) potassium hydrogen sulfate, (4) sirupy phosphoric acid, (*a*) distillation to approximately complete dehydration under reduced pressure, (*b*) distillation at ordinary pressure and maintaining the volume being distilled at 75 cc.

Some of these methods are discussed by Stilwell and Gladding,[1] particularly (4*a*). Withrow and Fritz[2] have modified the method of Stilwell and Gladding according to (4*b*).

The following additional facts were observed relative to these methods and their bearing on this problem: When proceeding according to (1) it was found necessary to add an excess of hydrochloric acid in order to sweep over the last portions of the acetic acid. By (2) and (3), sulfur dioxide was found present in the distillate, which introduced an appreciable error when the amount of oxalic acid in the oxidation solution was large. Carbon dioxide was present in the acetic acid distillate regardless of the method employed. When distilled with sirupy phosphoric acid under reduced pressure as in (4*a*), the solution of carbon dioxide in the condensate was avoided. Evans and Witzemann[3] have found that the loss of acetic acid by use of suction, was negligible when the acetic acid solution was very dilute. This was also the case in the experiments recorded in this paper. The distillation was much expedited by placing a second fractionating flask and a Kjeldahl connecting bulb between the distillation flask and the condenser, making it unnecessary to cool the contents of the distilling flask in order to prevent spattering on the addition of water to the hot mixture, as it was then extremely difficult for the phosphoric acid to reach the receiving vessel. The addition of water was made at the ordinary pressure in order to avoid the foaming, which otherwise occurred when the amount of alkali on the original sample was large.

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[1] THIS JOURNAL, 4, 105 (1882).

[2] Thesis by Howard Fritz of this laboratory.

[3] THIS JOURNAL, 34, 1091 (1912).

In (4*b*) the total volume of the distillate was not constant in quantity, as it was dependent upon the amount of acetic acid present in the sample. Inasmuch as the distillation was carried out at ordinary pressure, the carbon dioxide liberated was present in the condensate. Dr. Homer B. Adkins (this laboratory) found that bubbling carbon dioxide-free air through the distillate removed the undesirable gas without seriously affecting the quantity of acetic acid contained in these solutions of considerable dilution. In the following experiments on alcohol the same method was employed in eliminating the carbon dioxide. The distillate from methods (4*a*) and (4*b*) was titrated with a standardized potassium hydroxide solution with phenolphthalein as the indicator. In each experiment a correction was made for the volatile acids contained in the amounts of phosphoric acid used. It was observed in making these distillations that when the amount of potassium hydroxide present was large, a much greater excess of phosphoric acid over that required for the neutralization of the alkali, was necessary in order to completely expel the acetic acid, and also that the time required for the operation was decreased thereby.

(*b*) **Chemicals Used in the Oxidation.**—Absolute alcohol[1] was employed in these series of oxidations. Additional tests with phenyl-hydrazine and sodium hydroxide gave no turbidity, proving the absence of aldehydes. To obtain a pure product, commercial absolute alcohol was treated with calcium oxide in the customary way and then was stored with anhydrous copper sulfate in air-tight glass-stoppered bottles. In making up a standard solution sufficient alcohol (b. p. = 77.7° and 77.8°, at 739 and 749 mm.; $[d]^{20}_{4} = 0.7897$; $[d]^{25}_{4} = 0.7854$) was distilled from the copper sulfate to give a 2 *M* or 9.21% solution (92.096 g. anhydrous alcohol per liter of solution), having $[d]^{20}_{4} = 0.9830$ and $[d]^{25}_{4} = 0.9817$. These density values were referred to "Circular of the Bureau of Standards" No. 19, pp. 6 and 7, in order to get the per cent. by weight of alcohol present. An ordinary pyknometer (capacity about 60 cc.) was used in making these density determinations. All alcohol distillations were made in glassware, with cork connections.

Distilled water was aerated with carbon dioxide-free air for 5 to 6 hours. Carbon dioxide blanks were then run. One drop of 0 1017 *N* potassium hydroxide solution gave a permanent pink color to 100 cc. of the water containing one drop of phenolphthalein.

The oxidizing power of the potassium permanganate was established by titrating samples of about 0.13 g. each in solution against standard potassium tetroxalate solution. It was found to have a value of 98.67% of that required by theory.

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[1] Satisfying the requirements given in Merck, "Chemical Reagents, their Purity and Tests," 1914 edition

A potassium hydroxide solution containing 340.8 g. per liter (1 cc. = 0.004 g. carbon dioxide) was prepared and kept in a stock bottle.

(*c*) **Apparatus and Manipulation.**—Each oxidation which involved the addition of alkali was carried out as follows: The required amount potassium hydroxide solution was measured into a wide-mouth, 2-liter balloon flask, and made up to 1000 cc. with carbon dioxide-free water. When the alkalinity was less than 5.32 g. per liter (*v.* Table IV) about 1100 cc. of solution was prepared and small portions were titrated against standard sulfuric acid, to avoid any error due to the extensive dilution of a small volume (0.14 to 8.5 cc.) of the potassium hydroxide stock solution. 30.404 g. of crystallized potassium permanganate, equivalent to 30 g. of 100% salt, was next introduced, and the flask immediately closed by a rubber stopper into which was fitted a mercury sealed glass stirrer, a 25 cc. pipet and a piece of ordinary glass tubing, for the oxidations carried out at 25° and 50°. For the series at 75° and 100°, in addition to the above, an ordinary condenser provided with a soda-lime guard-tube was attached through the stopper by means of two adapter tubes. The closed vessel was next clamped in position in a bath which was kept at the desired temperature.

The thermostat bath was water for the 25° and 50° oxidations and paraffin for the 75° and 100° series. Heat was supplied by a large size "El Boilo" immersion heater. The amount of current flowing through the heater was automatically controlled by means of a mercury-toluene regulator and a lamp rheostat of considerable range. The temperature was held constant to within 0.15°.

When the desired temperatures of the flask and bath were reached and with the reaction mixture constantly stirred, 9.21% alcohol solution was slowly added drop by drop from a buret, loosely stoppered at the upper end, attached to the small glass tubing, until the reduction of the permanganate was complete. The end-point was determined by drawing a portion of the reaction mixture into the pipet, where, after the precipitated hydrated oxide or oxides of manganese had settled, the observations could be made. The color desired before discontinuing the addition of the alcohol in the case of the alkaline solutions was a very pale green, and in the neutral solutions was a delicate pink. This faint color was generally discharged within 24 hours through decomposition of the oxidizing agent.

Approximately the same color changes were observed by Chapman and Smith[1] in both their alkaline and neutral solutions. They stated "that the alkaline solution rapidly becomes green, and for a considerable time no binoxide of manganese is deposited," while it came down at once from the neutral solution. They made no reference to the weak alkaline

[1] *Loc. cit.*

solution. In solutions of high alkali concentration we found a light coat of the brown oxide of manganese on the surface almost immediately following the addition of the reducing agent.

The reaction mixture after being filtered in a carbon dioxide-free apparatus was made up to 2000 cc. and analyzed.

The 2-liter flask A containing the oxidation mixture was removed from the thermostat, placed on the rubber covered ring C and connected up as shown in Fig. 1. On the application of suction, and with the pinch-clamp F and screw-clamp H closed, the mixture was drawn from A into the glass jar E. The oxide of manganese was retained on the outside of the Pukal filter G while the filtrate passed on into the 2-liter suction flask. After a sufficient amount of material had been transferred to E, the clamp F was opened to stop transference. When the filtration and washing were complete, clamp H was opened and water sucked into the cell to wash the inside of it. The plate glass cover D and the vessel were ground and coated with vaseline so as to prevent leakage of air into the apparatus. Several

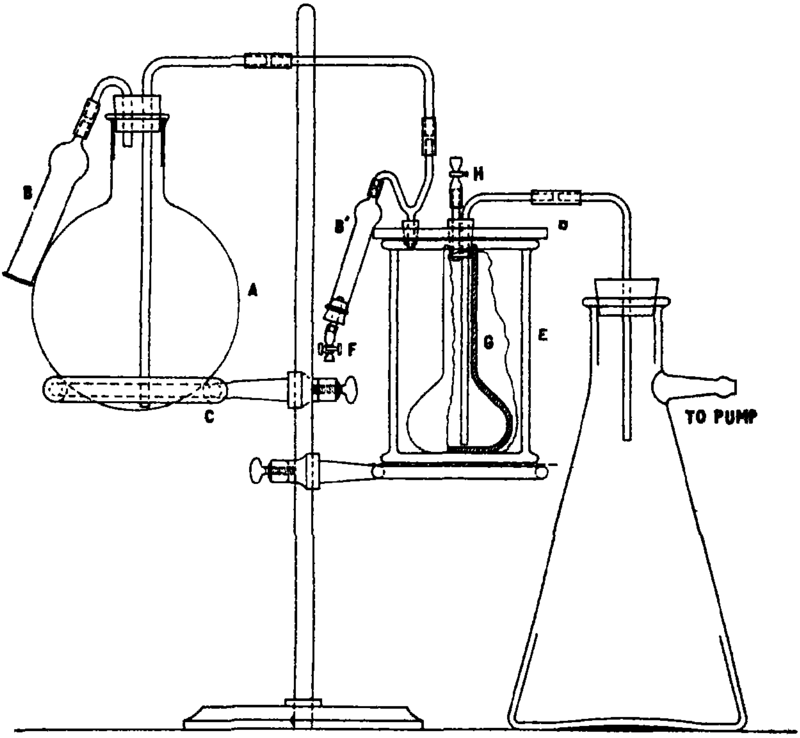

Fig. 1.

types of filters were tried, but the unglazed cell was found to be highly satisfactory, as a clean filtration and three washings were usually completed within 10 to 15 minutes. The cell was cleaned by first removing the main portion of the precipitate with a steel spatula, then was sponged off and finally treated with hydrochloric acid after which water was sucked through it until the washings were free from chlorides. To assure ourselves that no appreciable error was introduced due to absorption or possible adsorption by the Pukal filter, determinations were made on a filtrate containing the maximum amount of oxidation products obtained in the experiment.

(*d*) **Data.**—The results obtained from 4 series carried out at 25, 50, 75 and 100° are given in Tables I, II, III and IV, respectively. They are also represented in the form of curves as found in Figs. 2, *et. seq.* 30.404 g. of potassium permanganate was used in each experiment.

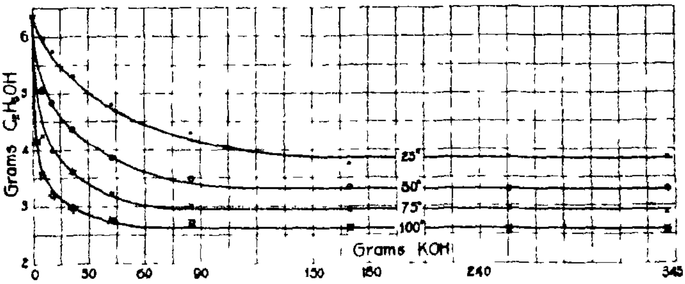

Fig. 2.

OXIDATION RESULTS.

TABLE I.

Temperature = 25°.

	Materials used. G.		Found, with proper correction for CO_2 and CH_3COOH. G.				Calculated for 4.605 g. alcohol. G.			
Col. 1.	2.	3	4.	5.	6	7.	8.	9.	10.	11.
Expt. No.	KOH.	C_2H_5OH.	CO_2	$(COOH)_2$		CH_3COOH.	CO_2.	$(COOH)_2$	CH_3COOH.	% yield.
1	0.00	6.37	0.00	0.000	0 00	8.17	0.00	0.000	5.91	98.43
2	5.32	5.95	0 581	0.401	59.80	7.03	0.450	0.310	5.44	99.16
3	10.65	5 72	0 845	0 869	49 30	6 21	0.680	0.700	5.00	98.78
4	21.30	5.30	1.02	0.912	46 94	5 17	0.890	1.05	4.49	96.58
5	42.60	4.82	1.08	1.60	40.69	4.44	1 03	1.53	4.24	99.33
6	85.20	4.30	1.22	2.09	37 35	3.60	1.14	1.95	3.86	98.90
7	170.4	3 74	0.942	1.71	35.96	3.04	1 16	2 11	3.75	99.09
8	255.6	3.85	0 866	1.81	34 00	3.18	1 06	2.17	3.80	99.43
9	340.8	3.86	0.964	1.75	36.09	3.16	1.15	2.09	3.77	99.06

TABLE II

Temperature = 50°

	Materials used. G.		Found with proper correction for CO_2 and CH_3COOH. G.				Calculated for 4.605 g. alcohol. G.			
Col. 1	2	3	4	5	6	7	8	9	10	11
Expt. No.	KOH	C_2H_5OH	CO_2	$(COOH)_2$		CH_3COOH	CO_2	$(COOH)_2$	CH_3COOH	% yield
10	0.00	6.40	0.00	0.00	0.00	8.17	0.00	0.00	5.87	97.76
11	5.32	5.05	1.04	1.07	50.00	4.99	0.95	0.98	4.55	97.48
12	10.65	4.77	1.39	1.64	46.30	4.02	1.34	1.58	3.88	97.42
13	21.30	4.37	1.45	1.96	43.22	3.33	1.53	2.06	3.51	98.74
14	42.60	3.85	1.49	2.12	41.71	2.50	1.78	2.53	2.99	98.13
15	85.20	3.48	1.33	2.15	38.78	2.09	1.76	2.84	2.77	97.68
16	170.4	3.35	1.32	2.18	38.13	1.96	1.81	3.00	2.70	98.89
17	255.6	3.30	1.35	2.24	38.12	1.84	1.88	3.12	2.57	98.82
18	340.8	3.30	1.32	2.10	38.90	1.98	1.84	2.93	2.77	99.61

TABLE III

Temperature = 75°

	Materials used. G.		Found with proper correction for CO_2 and CH_3COOH. G.				Calculated for 4.605 g. alcohol. G.			
Col. 1	2	3	4	5	6	7	8	9	10	11
Expt. No.	KOH	C_2H_5OH	CO_2	$(COOH)_2$		CH_3COOH	CO_2	$(COOH)_2$	CH_3COOH	% yield
19	0.00	6.38	0.00	0.00	0.00	8.24	0.00	0.00	5.95	99.11
20	5.32	4.25	1.38	2.19	43.21	3.22	1.50	2.02	3.49	97.61
21	10.65	3.97	1.58	2.10	43.30	2.60	1.83	2.44	3.02	98.20
22	21.30	3.62	1.65	2.33	42.01	2.00	2.10	2.96	2.54	99.04
23	42.60	3.20	1.65	2.40	41.35	1.46	2.38	3.45	2.10	100.34
24	85.20	3.03	1.63	2.41	40.84	1.19	2.47	3.66	1.81	98.89
25	170.4	2.93	1.65	2.34	41.80	1.09	2.59	3.68	1.71	98.80
26	255.6	2.95	1.57	2.38	40.20	1.17	2.45	3.71	1.83	99.46
27	340.8	2.88	1.58	2.28	41.39	1.11	2.52	3.64	1.78	98.72

TABLE IV

Temperature = 100°

	Materials used. G.		Found with proper correction for CO_2 and CH_3COOH. G.				Calculated for 4.605 g. alcohol. G.			
Col. 1	2	3	4	5	6	7	8	9	10	11
Expt. No.	KOH	C_2H_5OH	CO_2	$(COOH_2)$		CH_3COOH	CO_2	$(COOH)_2$	CH_3COOH	% yield
28	0.00	6.22	0.00	0.000	0.00	8.12	0.00	0.000	6.00	99.91
29	0.415	6.18	0.00	0.000	0.00	8.02	0.00	0.000	5.98	99.59
30	0.461	6.09	0.172	0.034	83.95	7.79	0.130	0.026	5.89	99.87
31	0.530	6.00	Undetd.	0.052		7.43		0.040	5.70	
32	0.662	5.81	0.504	0.341	60.23	6.96	0.400	0.270	5.52	99.46
33	0.863	5.65	0.981	0.767	56.65	6.14	0.800	0.625	5.00	99.30
34	2.66	4.14	1.20	1.99	38.00	3.20	1.33	2.21	3.56	98.96
35	5.32	3.54	1.33	2.21	38.13	2.19	1.73	2.87	2.85	99.02
36	10.65	3.22	1.52	2.32	40.00	1.63	2.17	3.32	2.33	100.37
37	21.30	2.97	1.64	2.39	41.30	1.17	2.55	3.71	1.81	100.34
38	42.60	2.75	1.69	2.36	42.20	0.86	2.83	3.96	1.44	100.14
39	85.20	2.72	1.78	2.47	42.30	0.685	3.01	4.19	1.16	100.08
40	170.4	2.64	1.81	2.45	43.02	0.539	3.16	4.28	0.940	99.13
41	255.6	2.57	1.77	2.39	43.04	0.508	3.17	4.29	0.910	98.85
42	340.8	2.58	1.98	2.23	47.53	0.515	3.54	3.99	0.920	99.89

Discussion.

Fig. 2 shows the number of grams of absolute alcohol required to reduce a constant weight of potassium permanganate at the 4 different temperatures and with increasing initial concentrations of the alkali. Beyond an alkalinity of about 100 g. (cf. Fig. 10) per liter of water, an increase in the initial concentration of the potassium hydroxide had little further effect on the amount of alcohol necessary to reduce the potassium permanganate completely. The curves showing the amounts of the oxidation products in Figs 3, 4, 5 and 6 are plotted on the basis of a constant quantity of alcohol (4.605 g. or 0.1 molecule). Figs. 7, 8 and 9 show the acetic, oxalic and carbonic acid curves for the 4 temperatures, respectively, and are represented on the same basis.

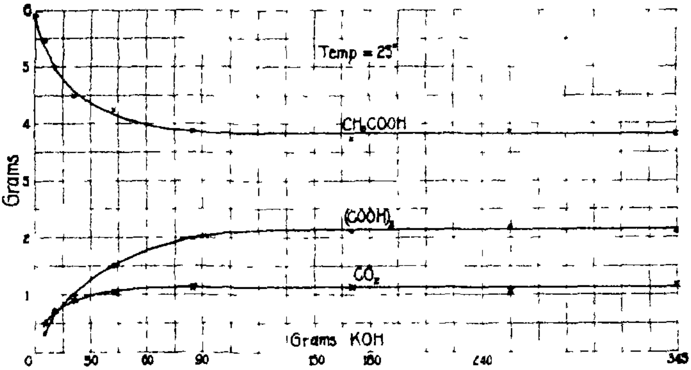

Fig 3

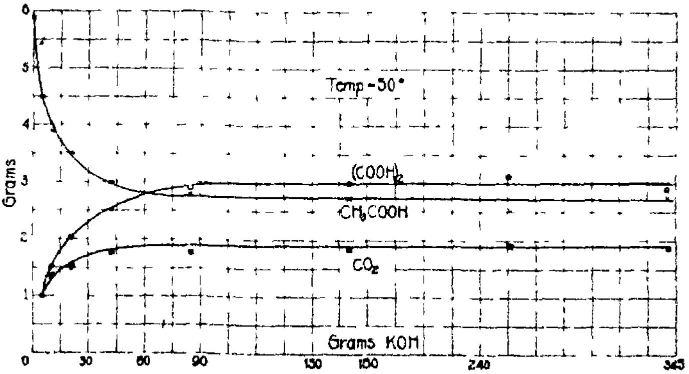

Fig. 4.

(*a*) **Oxidation Products.**—In the neutral reactions, acetic acid was the only substance found in quantities estimable by the common analytical methods. Chapman and Smith[1] oxidized alcohol with alkaline potassium permanganate and obtained acetic aldehyde, acetic acid, "together with various other bodies and oxalic acid." The difference in our experiments between the yields of alcohol as accounted for in the form of oxidation products and 100% might, in some cases, be construed as "various other bodies" The Jones test did not indicate any formic acid or formaldehyde. For a number of years the purity of alcohol has been determined by its oxidation to acetic acid by means of a chromic acid mixture.[2]

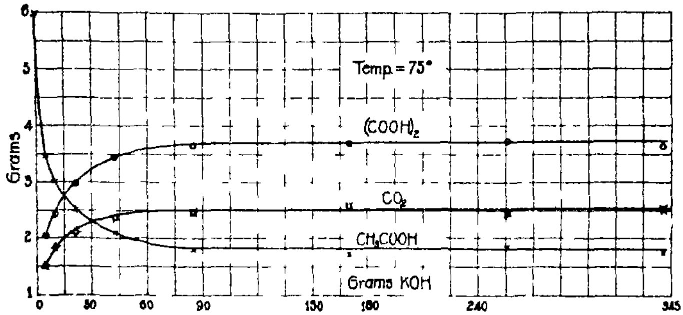

Fig. 5

Dr. Homer B. Adkins and one of us have shown that acetaldehyde is readily oxidized under the conditions used in this research. Hence, the amount of acetaldehyde, if present, must have been small. If other substances than acetic acid were present, the amounts were too small to allow detection. Denis[3] obtained only acetic acid in her experiments.

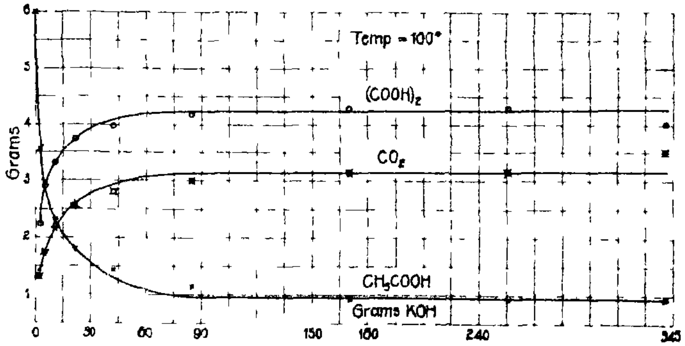

Fig 6.

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[1] *Loc. cit.*

[2] Chapman and Thorp, *J Chem Soc.*, 19, 482–3 (1866).

[3] *Am. Chem. J.*, 38, 564, 569–571 (1910).

It is interesting to note that when Voisenet[1] oxidized alcohol with the oxides of nitrogen, he obtained formaldehyde as a product of the reaction.

The yields of alcohol accounted for as oxidation products (Col. 11, Tables I, II, III and IV) are between 97.42 and 100 37%. In general, the yields of the 100° experiments came nearer totalling 100% than any of the others This does not necessarily mean that the 100° results should be accorded greater weight than the others. The low yield may have been due to incomplete oxidation or loss of the alcohol itself by evaporation from our reagent bottle The latter is hardly possible because specific-gravity determinations of the alcoholic solution were made about every 5 days and at no time was there a difference of more than one or two in the fourth place. At the temperature of 75° and 100°, it was thought that there might be a slow but appreciable evaporation of alcohol while the drops were travelling from the end of the dropping tube to the oxidation mixture (a distance of 8-10 cm.) To check up this possibility, the dropping tube was extended below the surface of the mix-

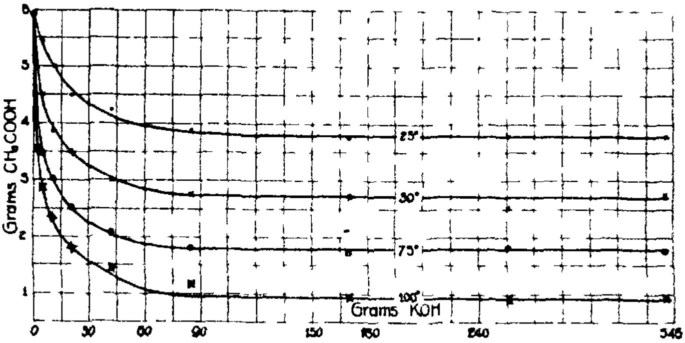

Fig 7.

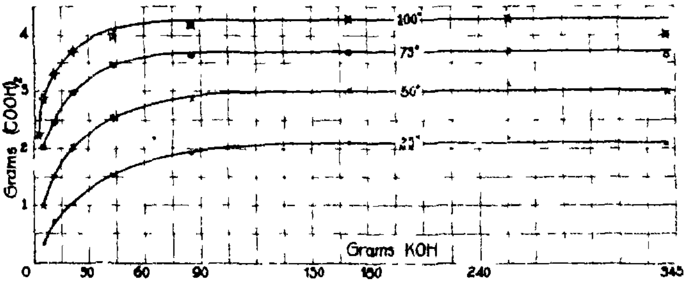

Fig 8

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[1] *Compt. rend*, 150, 40-43 (1910).

ture in the flask after which the repetition of all of the 75° series, and the last 5 of the 100° series, showed little or no difference in the amount of alcohol required for complete reaction from that used when the tube was of the shorter length.

Carbon Dioxide.—Only a trace was found in all our neutral experiments, and this was undoubtedly due to the unavoidable absorption of atmospheric carbon dioxide.[1] A correction for the carbon dioxide content of the reagents was always made. Test experiments showed that the mercury seals on the stirrers were effective in preventing the circulation of the air.

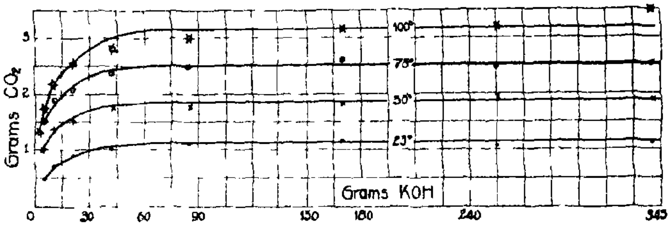

Fig 9

The formation of carbon dioxide in the alkaline experiments might be attributed to the following causes: (1) oxidation of acetates or (2) formates formed in the reaction; (3) decomposition of the oxalates formed and subsequent oxidation; (4) oxidation of the intermediate compounds arising from the dissociation of the oxidation products of alcohol. That the presence of carbon dioxide cannot be due to the decomposition of the acetates is abundantly borne out by the many instances in the literature of the stability of acetates in alkaline potassium permanganate solutions. Chapman and Smith found that oxalates were also totally unaffected in boiling solutions of potassium hydroxide and potassium permanganate. Hence, the presence of the carbon dioxide cannot be due to any action between the acetates and oxalates and the alkaline potassium permanganate Therefore, possibilities (1) and (3) are rigidly excluded.[2] The presence of carbon dioxide might be due to the intermediate formation of formates, as indicated by the work of Truchot,[3] who showed that formic acid is converted quantitatively into carbon dioxide in alkaline potassium permanganate solutions. Heimrod and Levene[4] explained the oxidation of acetaldehyde in alkaline solutions on the ground that formic acid is one of the reaction products. In view of the above facts, if formic acid is considered as an intermediate reaction product, it must be the decomposition product of a substance obtained from the acetaldehyde formed in the reaction. It will be shown below that it is not absolutely essential to postulate the formation of formic acid in order to account for the presence of carbon dioxide.

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[1] *Cf* Denis, *Am Chem J*, 38, 564, 571 (1907).

[2] Evans and Witzemann, THIS JOURNAL, 34, 1096 (1912).

[3] *Compt. rend.*, 63, 274 (1866).

[4] *Biochem. Z.*, 29, 49 (1910).

Oxalic Acid.—When the oxidations, with the exception of Expt. 30, were carried on in the presence of various initial concentrations of potassium hydroxide, oxalic and carbonic acids were formed with the acetic. Similar observations were made by Evans and Witzemann[1] in their experiments on the oxidation of propylene glycol, lactic acid, and pyruvic acid by means of alkaline potassium permanganate. Cochenhausen[2] also made similar observations in his work on the oxidation of acetone. Denis[3] found that acetic, oxalic and carbonic acids were the reaction products when alcohol is oxidized with alkaline potassium permanganate, a type of reaction which, in the present work, we have studied under definitely chosen conditions.[4] The amounts of the oxalic, carbonic and acetic acids obtained in the oxidation of ethyl alcohol at 50° have been expressed in our preliminary report as functions of the initial concentration of the alkali employed. In a recent study of the oxidation of acetone by means of alkaline potassium permanganate, Witzemann[5] has expressed his results in a somewhat similar manner.

The formation of the oxalic acid may be due to the following possible causes: (5) oxidation of any acetates or (6) formates formed in the reaction; (7) oxidation of intermediate compounds formed from acetaldehyde. Denis[6] studied the effect of an excess of potassium permanganate on acetic acid in the presence of potassium hydroxide at 100°, and found that no reduction took place. Wanklyn and Cooper,[7] on heating acetates with a considerable excess of alkaline potassium permanganate at a temperature of 160–180° in the presence of manganese dioxide, obtained potassium carbonate. When manganese dioxide was not added, oxygen was evolved. Barendrecht[3] did not detect any reaction between boiling strongly alkaline permanganate and acetic acid. Sodium acetate, according to Lossen,[8] was partially converted into sodium oxalate when heated with sodium hydroxide, potassium permanganate and a small amount of water. Truchot[3] made the observation that potassium permanganate had no effect on acetic acid in the presence of potassium hydroxide. These facts indicate that oxalic acid is not formed by the oxidation of acetic acid.

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[1] This Journal, 34, 1086 (1912).

[2] *J. prakt. Chem.*, [2] 58, 454 (1898).

[3] *Loc. cit.*

[4] See This Journal, 38, 377 (1916)

[5] *Ibid.*, 39, 2663 (1917).

[6] *Am. Chem. J.*, 38, 564 (1910).

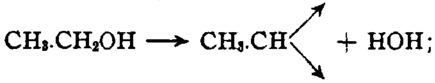
[7] *Phil. Mag.*, [5] 7, 138–140 (1879)

[8] *Ann.*, 148, 174–6 (1869).

Two drops of 0.089 *N* potassium permanganate solution were required to give a slight permanent color to the acetic acid distillate when it had previously been made alkaline with sodium carbonate, indicating the absence of formic acid. A blank containing the same amounts of acetic acid and sodium carbonate needed but one drop to give a color of the same intensity. Had formic acid been one of the intermediate reaction products, it would have been immediately oxidized to carbon dioxide as shown above. Hence oxalic acid is not formed by the oxidation of formic acid. It is true, however, that formic acid has been oxidized to oxalic acid by means of nitric acid.[1]

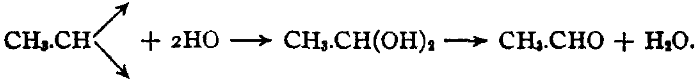
It is apparent, therefore, that the oxalic acid is formed in alkaline solution from the reaction compound of acetaldehyde.[2] On the basis of this research and those of other investigators, this explanation must be accepted as the correct one

Nef[3] and Denis[4] assume that the course of the reaction is as follows: Alcohol is dissociated into ethylidene and water.



$$CH_3.CH_2OH \longrightarrow CH_3.CH\begin{smallmatrix}\nearrow\\ \searrow\end{smallmatrix} + HOH;$$

the ethylidene is oxidized to ethylidene dihydroxide,



$$CH_3.CH\begin{smallmatrix}\nearrow\\ \searrow\end{smallmatrix} + 2HO \longrightarrow CH_3.CH(OH)_2 \longrightarrow CH_3.CHO + H_2O.$$

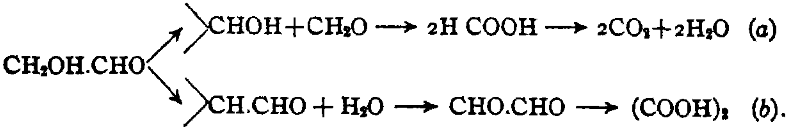
McLeod[5] has shown that acetaldehyde is converted into vinyl alcohol in the presence of alkali of a concentration of 0.10% or more; that is, the carbonyl group is enolized,

$$CH_3.CHO \longrightarrow CH_2 = CHOH;$$

the vinyl alcohol is then converted to glycollic aldehyde,

$$CH_2 = CHOH + 2HO \longrightarrow CH_2OH.CH(OH)_2 \longrightarrow CH_2OH.CHO + H_2O.$$

The glycollic aldehyde then undergoes a dissociation as expressed by the following.



$$CH_2OH.CHO\begin{cases}\nearrow\rangle CHOH + CH_2O \longrightarrow 2H\,COOH \longrightarrow 2CO_2 + 2H_2O & (a)\\ \searrow\rangle CH.CHO + H_2O \longrightarrow CHO.CHO \longrightarrow (COOH)_2 & (b).\end{cases}$$

[1] Weyl, *Ber.*, 17, 9 (1883).

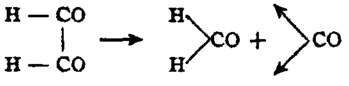
[2] Homer Adkins and one of us have completed work on acetaldehyde which we hope to publish in the near future.

[3] *Ann.*, 298, 315, 319 (1897).

[4] *Am. Chem. J.*, 38, 563–7 (1907).

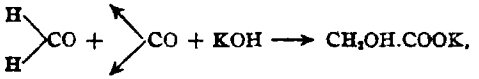
[5] *Ibid.*, 37, 25 (1907).

Such an interpretation would readily explain the presence of both oxalic and carbonic acids in alkaline solutions. It has been shown by Adkins and one of us that in alkaline solutions of potassium permanganate glyoxal is oxidized to both oxalic acid and carbonic acid, hence possibility (*a*) is not really essential for an understanding of these reactions. As is well known, the 1,2-diketo compounds[1] can readily undergo the benzilic acid rearrangement as follows:



$$\begin{matrix}H-CO\\ |\\ H-CO\end{matrix} \longrightarrow {}^{H}_{H}\!\!>CO + \;>CO \qquad (c)$$

then in the presence of alkali,



$${}^{H}_{H}\!\!>CO + \;>CO + KOH \longrightarrow CH_2OH.COOK, \qquad (d)$$

which compound, as has been shown by Adkins and one of us, is oxidized to oxalic acid and carbon dioxide by alkaline potassium permanganate. That glyoxal is converted to glycollic acid in cold alkalies is a well known fact. This reaction is analogous to the conversion of pyruvic aldehyde into lactic acid in alkaline solutions. Heimrod and Levene[2] give the following steps for the oxidation of acetaldehyde in alkaline solution: acetaldehyde ⟶ vinyl alcohol ⟶ glycollic aldehyde ⟶ glyoxal ⟶ formic acid and oxalic acid In view of these facts it is apparent that the presence of formic acid does not necessarily explain the presence of carbon dioxide in these reactions.

In this connection it is interesting to note that in the experiment of Denis[2] on the oxidation of ethyl alcohol in alkaline potassium permanganate solution, the ratio of the alcoholic equivalent of carbon dioxide to that of oxalic acid is as 12.6%: 7.6%, *i. e.*, the alcoholic equivalent of carbon dioxide is 62.5% of the total as carbon dioxide and oxalic acid. In the oxidation of acetaldehyde under approximately the same conditions the ratio of the acetaldehyde equivalent of carbon dioxide to that of oxalic acid is as 17%: 9.2% or the acetaldehyde equivalent of carbon dioxide is 64% of the total as carbon dioxide and oxalic acid. Col. 6 in the "Oxidation Results," gives similar information for our work on alcohol.

(*b*) **Effect of Variation of Initial Concentration of Alkali.**—This effect on the character of the oxidation products at 25, 50, 75 and 100° is shown in Figs, 3, 4, 5 and 6, respectively. In general, an increase in the initial concentration of the alkali causes an increase in the oxalic acid and carbon dioxide production, and a decrease in the acetic acid production. An examination of the curves shows that the yields of these acids reach approximately a constant value for a given temperature when the initial concentration of the alkali is about 100 g. per liter. The lowest initial concentration of potassium hydroxide employed at 25, 50 and 75° was 5.3 g. per liter. At this concentration oxalic acid and carbon dioxide were found at all 3 temperatures. At 100° the lowest possible initial concentration of alkali necessary for the production of oxalic acid in appreciable amounts was found to lie between 0.415 and 0.461 g. of potassium hydroxide (Expts. 29 and 30).

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[1] Cf. *Am. Chem. J.*, 35, 116 (1906).

[2] *Loc. cit.*

In Fig. 10 the logarithms of the acetic acid production are plotted against the logarithms of the initial concentration of the potassium hydroxide. The general equation for these lines is

$$y = \frac{B}{x^a}$$

where y is the concentration of the acetic acid obtained, x is the initial concentration of the potassium hydroxide, a is the tangent of the line and B is a constant. The values of a given below were obtained directly from Fig. 10 by measurement. To derive B we may use the equation

$$\log y = \log B - a \log x; \text{ thus,}$$

Temperature	B	a
25°	6.74	0.1227
50°	6.20	0.1839
75°	5.41	0.2459
100°	4.74	0.3084

Knowing the values of B and a, it is easy to calculate the maximum alkali concentration which will still give the theoretical yield of acetic acid. This value was found to be as follows:

Temperature	Alkali concentration
25°	2.55
50°	1.19
75°	0.655
100°	0.460

As noted above, we found that the value at 100° must lie between 0.415 and 0.461 g., while our calculation shows that the amount of alkali is 0.46 g. These values mean that at any concentration of alkali greater than those given, acetic acid production will diminish and oxalic acid and carbon dioxide will begin to form.[1] It is therefore to be concluded that one of the marked effects of an increase in the alkali concentration must be to increase the concentration of vinyl alcohol.

It is evident that the results of any two oxidations at a given temperature will afford a means of obtaining both the value of a and the maximum alkali concentrations that may be used in obtaining the theoretical yield of acetic acid. If y' and x' are the data obtained in a second oxidation, y the theoretical yield (*i. e.*, 6.003 g. of acetic acid), then x, the alkali concentration, may be calculated from the following equations:

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[1] McLeod, *Am. Chem. J.*, 37, 24 (1907).

$$\log y - \log y' = a\,(\log x' - \log x)$$

or

$$\frac{\log y - \log y' - a \log x'}{a} = -\log x.$$

(*c*) **Effect of Temperature.**—It was found that the temperature also has a twofold effect in these oxidations; namely, to increase the speed of the oxidation, and to modify the character of the reaction products. The general effect of temperature on the production of acetic, oxalic and carbonic acids, is shown in Figs. 7, 8 and 9, which shows that the acetic acid production falls off rapidly with the temperature while that of oxalic and carbonic acids increases with the temperature.

The fact that less alcohol was required for complete reduction at 100° (excluding neutral solution) than at the lower temperatures, means that more permanganate would have been required for the same amount of alcohol In other words, the quantitative conversion of alcohol into oxalic and carbonic acids becomes more nearly complete at higher temperatures and in the presence of more of the oxidizing agent. Barendrecht employed a temperature of approximately 100° for his work. Kastle and Loevenhart found that an increase in temperature accelerated the reaction between formaldehyde and hydrogen peroxide.

Hetper[1] states that when ethyl alcohol is oxidized with alkaline potassium permanganate, the temperature requisite for a theoretical yield of acetic acid must be below 0°. This conclusion is not warranted, as can be seen from the discussion of Fig. 10, where it is shown that acetic acid is the only product formed with low potassium hydroxide concentrations.

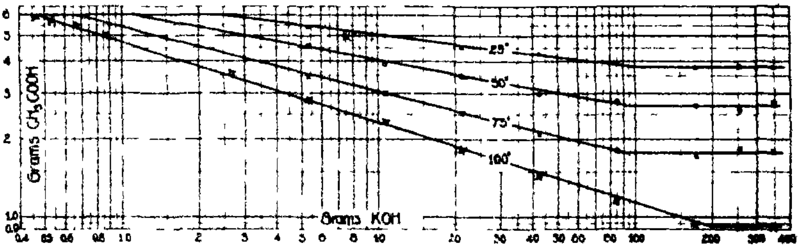

Fig. 10.

In Fig. 11 the tangents of the acetic acid log curves are plotted against temperature. A straight line passed through the 4 points cuts the *Y*-axis at a point near —25°. At this temperature the slope of the acetic acid curve is *zero*. If, *e. g.*, $x = 300$ when $a = 0$, by substitution in $\log B = \log y + a \log x$, the last term becomes zero, and $B = y = 6.003$, which is the theoretical yield in g. of acetic acid from 4.604 g. ethyl alcohol. This means that at the temperature indicated by the intersection of the line of tangents and the Y-axis the concentration of the alkali does not affect the theoretical yield of acetic acid.

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[1] *Z. anal. Chem.*, 51, 415 (1912)

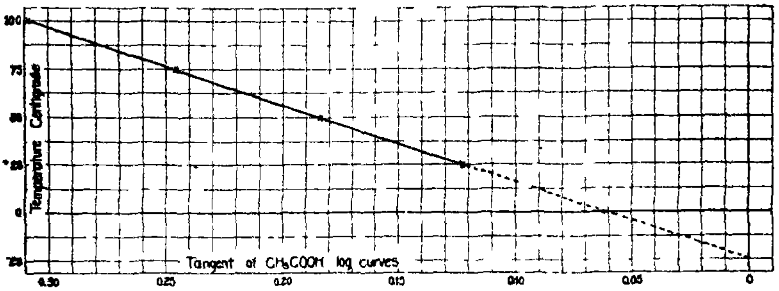

Fig 11

It has been repeatedly observed in these experiments that the rate of adding the alcoholic solution had no appreciable influence on the relative quantities of the oxidation products.

Summary.

1. In neutral aqueous solutions of potassium permanganate at temperatures of 25, 50, 75 and 100°, the sole reaction product of the oxidation of ethyl alcohol is acetic acid.

2. (*a*) When ethyl alcohol is oxidized at the temperature of 25, 50 and 75° by means of alkaline potassium permanganate solution containing 5.32 to 340 8 g. potassium hydroxide per liter, the reaction products are acetic, oxalic and carbonic acids, (*b*) when ethyl alcohol is oxidized at 100° by means of potassium permanganate in the presence of 0.415 g. potassium hydroxide per liter of solution, the product is still acetic acid, but when the alkalinity was from 0 461 to 340 8 g. per liter, oxalic and carbonic acids were present in addition to the acetic acid.

3. The oxidation of ethyl alcohol by means of alkaline (*v.* Summary No. 2) potassium permanganate at the above temperatures is accompanied by a diminution in the yield of acetic acid and a corresponding increase in the yield of oxalic acid and carbonic acids as the concentration of the alkali was increased up to the beginning of the maximum effect.

4. (*a*) An increase in the temperature of the alkaline reaction mixture (excluding Expt. 29) diminishes the yield of acetic acid proportionately; (*b*) an increase in the temperature of the alkaline reaction mixture (excluding Expt. 29) increases the yield of oxalic and carbonic acids proportionately.

5. An increase in the temperature of the reaction mixture hastens the rate of oxidation.

6. An increase in the alkalinity of the reaction mixture, up to a certain maximum amount, increases the rate of oxidation.

7. A comparison between the results of two experiments recorded by Denis is given.

8. The rate of the addition of the alcoholic solution has no effect on the relative amounts of the oxidation products so far as could be ascertained.

9. An equation has been developed for the relationship between the acetic acid production and the initial concentration of the alkali used when alcohol is oxidized at a given temperature in the presence of potassium hydroxide.

10. By means of this equation it is easy to establish the upper limit of the alkali concentration permitted and still obtain a theoretical yield of acetic acid, *i. e.*, the lower limit of alkali concentration at which oxalic acid forms.

11. By means of this equation it can be shown that at —25° the magnitude of the initial concentration of the potassium hydroxide used would not affect a quantitative yield of acetic acid.

12. An apparatus has been described for the filtering of sludge precipitates in the absence of the carbon dioxide of the air.

COLUMBUS, OHIO

[CONTRIBUTION FROM THE CHEMICAL RESEARCH LABORATORY, THE UPJOHN COMPANY.]

THE YELLOW COLORING SUBSTANCES OF RAGWEED POLLEN.

BY FREDERICK W. HEYL.

Received May 26, 1919.

These coloring substances belong to the flavonols and are entirely glucosidic. They are extracted with alcohol, and after preparing an aqueous solution from this alcoholic extract a complete precipitation may be secured with basic lead acetate. The yield amounts to about 7.0 g. from 1150 g. pollen or approximately 0.6%.

The least soluble of these was identified as a quercitin glucoside having the composition $C_{21}H_{20}O_{12}$ and melting at 228–9°. The only sugar obtained upon hydrolysis was glucose. It is therefore isomeric with, and differs from, quercimeritrin and isoquercitrin, which were first isolated by A. G. Perkin[1] from the flowers of *Gossypium herbaceum*. These melt, respectively, at 247–249° and 217–219°. One other isomer is known, having been isolated by Rogerson[2] from the flowers of *Trifolium incarnatum*. Incarnatin melts at 242–245°. The most characteristic behavior of pollen quercitin glucoside on melting is the sharp formation of a cherry-red oil at the melting point, a peculiarity not noted with any of the above mentioned isomers.

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[1] *J. Chem. Soc.*, **95**, 2181 (1909); Viehoever, Chernoff and Johns, *C. A.*, **12**, 1562 (1918).

[2] *J. Chem. Soc.*, **97**, 1008 (1910).

The more soluble fractions of the mixed glucosides contained a glucoside of isorhamnetin. This fraction yielded magnificent crystals of hexagonal prisms, but these were extremely soluble; 2–3 cc. of warm water dissolving a gram or more and yielding a thick unfilterable crystalline mush. Upon hydrolysis it gave isorhamnetin, $C_{16}H_{12}O_7$, a monomethyl derivative of quercitin, and yielded the characteristic beautifully crystalline tetraacetyl-isorhamnetin melting at 197–200°. This substance has been previously isolated[1] from the flowers of *Cheiranthus cheiri* and from red clover flowers.[2] The glucoside of isorhamnetin appears to predominate.

Experimental Part.

Ragweed pollen (approximately 1150 g.) which had been percolated with ether to remove fat, was percolated with alcohol (94%–98%) until the percolate was almost free from color. After distilling off most of the alcohol under diminished pressure this extract was mixed with distilled water and the resin that separated was removed. The aqueous liquor was extracted with ether and the coloring substances were fractionally precipitated by 3 additions of basic lead acetate solution, the yellow precipitates being removed on a Büchner filter, washed with water, and decomposed with hydrogen sulfide, yielding 3 fractions.

On concentrating Fraction I (50 cc.) and cooling, a substance separated in yellow globules. This material was dissolved in a mixture of pyridine and water (1 : 3) but no satisfactory crystallization resulted; on heating and adding an equal volume of glacial acetic acid the substance separated in a crystalline condition having the appearance of wheat. It was very impure, sintering below 170°, becoming soft at 185° and having completely decomposed to a red foam at about 195°. It was insoluble in ether or toluene, but dissolved in boiling nitrobenzene, failing to crystallize satisfactorily. It was purified by boiling with water, to which pyridine was added drop by drop until solution was effected and then collecting the crystals (light yellow needles) which separated from the hot solution. The melting point was raised as follows: 212–220°, 224°, 223–5°, and 224–6°, to a red oil. Yield (0.12 g.).

Subs. dried in vacuum at 130° 0.1174. CO_2, 0.2322; H_2O, 0.0466.

Calc. for $C_{21}H_{20}O_{12}$ C, 54.3; H, 4.3. Found. C, 53.95; H, 4.45.

The original aqueous solution from which the crude glucoside separated could be concentrated to a syrup without further crystallization. It contained a mixture of extremely soluble uncrystallizable glucosides. This syrup was taken up with 5% sulfuric acid and heated upon the steam bath until the separation of insoluble yellow substance was complete. This, when filtered off on a gooch crucible, weighed 1.097 g. It was discolored. It was redissolved in ammonium hydroxide solution and reprecipitated with hydrochloric acid. The precipitate was dissolved as far as possible in ether, and the ether solution was extracted with water, ammonium carbonate, and then with potassium carbonate, which took out a considerable part of the material in a deep orange colored solution. The last mentioned extract was acidified and the yellow precipitate filtered off on suction and washed with water. It melted with decomposition at 286°. It was recrystallized with dilute alcohol[1] from which it separated in microscopic crystals melting at 281–286° (C 58.3, H 3.75). The remainder was acetylated and the colorless acetyl derivative obtained proved to be comparatively soluble, most of it remaining in the mother liquor as a syrup. The crystalline part (0.05 g.) softened at 144° and melted at 148–149°. Upon recrystallization it softened at 146° and melted at 149–151°. The yellow substance therefore is not quercitin but a mixture.

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[1] A. G. Perkin, *J. Chem. Soc.*, 69, 1658 (1896).

[2] Power and Salway, *Ibid.*, 97, 245 (1910).

The yellow hydrolytic cleavage products having been filtered off, the filtrate after clarifying with lead subacetate showed the presence of 0.534 g. glucose by the Munson-Walker process. The phenylglucosazone melted at 203-4° and pentose sugars were absent, it being impossible to obtain even a trace of phloroglucide by the quantitative procedure.

Upon concentrating the filtrate from the lead sulfide after decomposing the *second lead salt* two crystalline deposits A and B, consisting chiefly of yellow globules, were obtained. A (1.1 g.), was repeatedly recrystallized from water but the melting point remained 170–211°. B (1.0 g.), when fractionally crystallized from water, gave a small crop of needles of the glucoside melting at 221–224°, but from the mother liquors material similar to A separated. By crystallization from water and pyridine a small yield of pure yellow glucoside (0.3 g.) melting at 222–5° was obtained from A, and B yielded the same product, m. p. 228–9°.

The glucoside here obtained was hydrolyzed with unsatisfactory results: 0.2733 g. was heated on the steam bath with dilute alcohol in a covered beaker in the presence of approximately 5% sulfuric acid, and with the occasional addition of alcohol. The solution was then concentrated and alcohol completely removed, several additions of water being made to keep the volume constant. After standing overnight, 0.1579 g. yellow cleavage product was filtered off on a gooch crucible (57.8%). The filtrate yielded pure *d*-phenyl-glucosazone melting at 205–6°.

[1] The mother liquors from this substance contained alteration products which were very soluble in water yielding red solutions that no longer gave yellow solutions with alkali. Potassium hydroxide intensified the red color.

The yellow cleavage product was twice crystallized from 95% alcohol and melted at 311–313°, but was not identical with the product later obtained which melted at 314–315°, as a mixture of the two melted at about 288°. After drying *in vacuo* at 130°, it was analyzed.

Subs., 0.0814: CO_2, 0.1773; H_2O, 0.0259.

Calc for $C_{15}H_{10}O_7$: C, 59.6; H, 3.3. Found: C, 59.4; H, 3.6.

The substance agrees in all its properties with quercitin. When mixed with quercitin from *Zygadenus* (m. p. 305°), the mixture melted at 305–7°. It yielded a colorless acetyl derivative that crystallized characteristically from alcohol and melted at 191–3°. When mixed with acetyl quercitin the melting point was not depressed.

Although the calculated yield of quercitin from the equation

$$C_{21}H_{20}O_{10} + H_2O = C_{15}H_{10}O_7 + C_6H_{12}O_6,$$

should be 65% (found 57.8), there is no doubt but that the substance is a quercitin glucoside.

The mother liquors (pyridine + water) which accumulated during the purification of this quercitin glucoside contained more than 0.5 g. glucosidic material. It was hydrolyzed and the yellow cleavage product converted into the colorless acetyl derivative. The crude product melted at 165–180° and after several recrystallizations at 188–195°. A methoxyl determination here indicated that it consisted of a mixture of acetylisorhamnetin and acetylquercitin, the former predominating.

Subs., 0.0511 (182–192°). AgI, 0.0170. Found: OCH_3, 4.4.

The filtrate from B upon concentration yielded 2.0 g. of an insoluble yellow product C as it was concentrated to a syrup, hydrolysis evidently being effected by a small amount of free acid present. The insoluble yellow cleavage product was filtered off and the filtrate made acid with 5% sulfuric acid to complete the hydrolysis and heated on the steam bath and again filtered from a further slight quantity of badly contaminated cleavage product. The acid filtrate on thorough examination contained nothing but glucose.

The product C (2.0 g.) was boiled twice with smaller volumes of water and then the insoluble residue was boiled with one liter of water and filtered hot. From the filtrate a small quantity (0.07 g.) of micro-crystalline material separated. Dried at 120°, it softened at 255° and melted to a black oil at 260°. It is readily soluble in ammonia, yielding a yellowish green color, which turned to a burnt yellow when the ammonia is expelled (C, 61.15; H, 3.9). It is probably the same material as the insoluble part.

The insoluble part was dissolved in boiling 95% alcohol, and water was added to opalescence and then on cooling the material separated in amorphous balls melting at 293–6°. It weighed 0.6 g. For further purification the material was acetylated with acetic anhydride in the presence of a drop of pyridine. By 5 crystallizations from alcohol the melting point of this colorless acetyl derivative that crystallized in needles was elevated from 191–2° to 197–200°.

Subs., 0.0667: CO_2, 0.1444; H_2O, 0.0247.

Subs., 0.0921: AgI, 0.0466.

Calc. for $C_{16}H_8O_7(COCH_3)_4$ C, 59.5; H, 4.1; OCH_3, 6.4. Found: C, 59.05; H, 4.15; OCH_3, 6.7.

The pure acetyl derivative was hydrolyzed by boiling with 5% sulfuric acid in dilute alcohol and filtering after removing the alcohol on the steam bath. The recovered yellow substance separated from 95% alcohol in curved prims and melted sharply at 314–315° to a black oil.

Subs., 0.079: CO_2, 0.1768; H_2O, 0.0288.

Calc. for $C_{16}H_{12}O_7$: C, 60.7; H, 3.8. Found: C, 61.05; H, 4.1.

This substance appears to be isorhamnetin, one of the monomethyl quercitins, and the purification through the acetyl derivative did not change the results of the combustion.

The *third lead precipitate* was decomposed with hydrogen sulfide and the filtrate from the lead sulfide was concentrated to a syrup but no crystals resulted. The syrup, when subjected to acid hydrolysis, yielded only calcium sulfate.

The writer is greatly indebted to Mr. Clayre Pomeroy for the analytical work.

KALAMAZOO, MICH.

[CONTRIBUTION FROM THE MELLON INSTITUTE AND THE SCHOOL OF CHEMISTRY, UNIVERSITY OF PITTSBURGH.]

PHTHALIC ACID DERIVATIVES; CONSTITUTION AND COLOR. XVI.[1] PHENOLTETRABROMO-PHTHALEIN AND SOME OF ITS DERIVATIVES.

BY DAVID S. PRATT, F. B. DOANE AND A. W. HARVEY.

Received May 31, 1919.

The preparation of various halogenated phenolphthaleins has been considered important from two standpoints, *i. e.*, to provide additional indicators of this excellent type for analytical work and to further our knowledge of the effect on absorption spectra brought about by the substitution of important atoms in phthalic acid derivatives. Since the corresponding chlorine and iodine derivatives of phenolphthalein have been prepared it was interesting to study the intermediary bromine analogues.

Phenoltetrabromo-phthalein with the halogen in the anhydride ring was probably obtained in an impure condition by Rupp,[2] but details are lacking in his brief report. The phthalein and some of its more important derivatives have now been prepared in a condition of purity sufficient even for spectroscopic investigation. Unfortunately it is not possible to make this part of the contemplated study at the present time. For this reason the various probable effects due to introducing 4 bromine atoms possessing an acidity between chlorine and iodine and with characteristic activity on adjacent points of unsaturation will not be discussed until spectroscopic data are available.

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[1] THIS JOURNAL, 40, 1425 (1918).

[2] *Arch. Pharm.*, 249, 56 (1911).

The tetrabromo-phthalic anhydride used was prepared by the convenient method outlined in a previous article.[1]

Phenoltetrabromo-phthalein.—464 g. of tetrabromo-phthalic anhydride was placed in a 2-liter, round-bottom flask provided with an air condenser and intimately mixed with 1390 g. of freshly distilled phenol. The temperature was raised to about 50° C. and 450 g. of fuming sulfuric acid (15% SO_3) added gradually as the reaction proceeded Heat was then applied by means of an electrically heated air bath at 160° for 9 hours, during which the color of the mix changed nearly to black.

The hot reaction product was poured into a large volume of boiling water, washed several times by decantation and finally steamed thoroughly for several hours or until the odor of phenol had largely disappeared. The material was dissolved in dil. sodium hydroxide solution, precipitated hot with dil. hydrochloric acid, filtered, and washed free from chlorides. The phthalein in the dried product was extracted with alcohol in which unchanged anhydride and tetrabromo-fluoran are insoluble. The residue obtained by distilling off the alcohol contained some tar, and was therefore dissolved in glacial acetic acid and thoroughly treated with bone black. Faintly yellow crystals were deposited on concentration and cooling, giving a yield of 75% of the theoretical amount. Too rapid heating during condensation or prolonged time at high temperature causes excessive tar formation.

The phthalein was further purified by repeated alternate recrystallization from alcohol and glacial acetic acid until finally obtained in nearly colorless crystals. It is quite soluble, without color, in ordinary organic solvents, and very sensitive to alkali, giving deep purplish red solutions. Ammonia, however, either dry or moist, failed to give the corresponding salt when passed over the dry phthalein. Halogen in every case was determined by the modified lime combustion method.

Subs., (I) 0.3023; (II) 0.2912. Cc. 0.1 N $AgNO_3$: (I) 19.10; (II) 18.34.

Calc. for $C_{20}H_{10}O_4Br_4$: Br, 50.43. Found: (I) 50.50; (II) 50.34.

The structure of phenoltetrabromo-phthalein is undoubtedly represented correctly as

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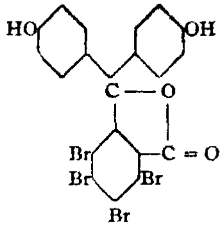
[1] This Journal, 40, 1416 (1918).



Tetrabromo-fluoran.—The residue left after extracting the crude reaction product with alcohol consisted largely of unchanged anhydride and tetrabromo-fluoran. The former was removed by treating with warm dil. sodium hydroxide solution. The fluoran remaining was washed and purified by repeated recrystallization with bone black from glacial acid in which it is sparingly soluble, being finally obtained as well defined colorless crystals.

Subs., (I) 0.3175, (II) 0.3356 Cc. 0.1 N $AgNO_3$ (I) 20.55, (II) 21.83
Calc. for $C_{20}H_8O_3Br_4$ Br, 51.91 Found (I) 51.74, (II) 51.98

Phenoltetrabromo-phthalein Diacetate.—The diacetate was prepared by boiling for one hour a mixture of 15 g. of the pure phthalein, 9 g. of fused sodium acetate, and 45 cc. of acetic anhydride. The impure acetate was dissolved in benzene containing acetic anhydride, boiled with bone black for many hours, and finally recrystallized from benzene and alcohol. A yield of pure colorless, well formed crystals corresponding to 65%, was obtained.

Subs., (I) 0.2716, (II) 0.4026 Cc. 0.1 N $AgNO_3$ (I) 15.13, (II) 22.48
Calc. for $C_{24}H_{14}O_6Br_4$ Br, 44.53 Found (I) 44.42, (II) 44.62

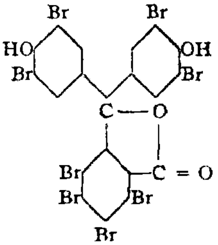
Phenoltetrabromo-phthalein Dibenzoate.—The dibenzoate was prepared by dissolving the pure phthalein in 2% sodium hydroxide solution and shaking with successive portions of benzoyl chloride until the red color disappeared. The product was washed with dilute alkali and 50% alcohol, and recrystallized several times from alcohol. A yield representing 80% was obtained as fine, colorless needles readily soluble in benzene, less so in alcohol.

Subs., (I) 0.2726, (II) 0.2244. Cc. 0.1 N $AgNO_3$ (I) 12.84, (II) 10.58
Calc. for $C_{34}H_{18}O_6Br_4$ Br, 37.97. Found (I) 37.81, (II) 37.69

Phenoltetrabromo-phthalein Dimethyl Ether.—15 g. of the pure phthalein was dissolved in 5% sodium hydroxide solution and shaken with successive small portions of dimethyl sulfate. The purple color gradually disappeared and the crude ether precipitated in a yellow amorphous condition. This was purified from alcohol and obtained as colorless crystals which tended to become pale salmon color on drying.

Subs., (I) 0.3217; (II) 0.3026 Cc. 0.1 N $AgNO_3$ (I) 19.44; (II) 18.18.
Calc. for $C_{22}H_{14}O_4Br_4$: Br, 48.30. Found: (I) 48.12; (II) 48.01.

Tetrabromophenol-tetrabromophthalein.—A solution of 10 g. of bromine in 25 cc. of alcohol was added through a reflux condenser to a boiling solution containing 10 g. of pure phenoltetrabromo-phthalein in 75 cc. of alcohol. Yellow crystals separated at once, the reaction being complete by the time all the bromine was added. A theoretical yield was obtained. The crude product was purified by recrystallization from acetone, giving very pale yellow crystals very slightly soluble in alcohol, easily in acetone. Aqueous alkali dissolves the phthalein with a brilliant clear blue color. Spectroscopic analysis will probably show that the yellow color is due to shifting the limit of visible general absorption toward the longer wave lengths sufficiently to make it evident to the eye. It is exactly these progressive shiftings in the absorption bands that will be investigated when the essential apparatus becomes available. There are no facts, however, opposed to the usual benzenoid structure which should therefore be represented as



Subs , (I) 0 2575, (II) 0 2291 Cc 0 1 N $AgNO_3$ (I) 21 63, (II) 19 29
Calc for $C_{20}H_6O_4Br_8$ Br, 67 34 Found (I) 67 14, (II) 67 25

Diammonium Salt.—Exposure of a weighed quantity of the phthalein to dry ammonia caused the color to become turquoise blue with a gain in weight corresponding to two molecules of ammonia. The salt is not very stable even at ordinary temperatures, and loses its ammonia quantitatively at 100°.

Subs., 0 8047 (I) gain in weight, 0 0283, (II) loss in weight, 0 0282
Calc for $C_{20}H_6O_4Br_8\ 2NH_3$ NH_3, 3 46 Found. (I) 3.43; (II) 3 40

Tetrabromophenol-tetrabromophthalein Diacetate.— 10 g. of pure phthalein was boiled for one hour in 35 cc. of acetic anhydride containing 8 g. of fused sodium acetate The hot solution was poured on ice and the crude acetate washed thoroughly with water. It was purified from benzene containing acetic anhydride. The colorless crystals so obtained contained a molecule of benzene removable by heating at 175°.

Subs , 0 6269. Loss in weight, 0 0472
Calc for $C_{24}H_{10}O_6Br_8\ C_6H_6$ C_6H_6, 7.02. Found: 7.52.
Subs., (I) 0.2352; (II) 0 2515 Cc. 0.1 N $AgNO_3$: (I) 18.14; (II) 19.44.
Calc. for $C_{24}H_{10}O_6Br_8$ Br, 61 86. Found (I) 61.64; (II) 61 79.

Tetrabromophenol-tetrabromophthalein Dibenzoate. — The dibenzoate was prepared in a similar manner to that used for phenoltetrabromophthalein dibenzoate. The colorless crystals obtained after treating with bone black a benzene solution contained a molecule of solvent which was slowly driven off at 130°.

Subs, 0.9861. Loss in weight 0 0580
Calc. for $C_{34}H_{14}O_5Br_8\ C_6H_6$ C_6H_6, 6 31 Found 5 89
Subs, (I) 0 2520, (II) 0 2763 Cc 0 1 *N* $AgNO_3$ (I) 17 25, (II) 19 08
Calc. for $C_{34}H_{14}O_6Br_8$ Br, 55 23 Found (I) 54 70, (II) 55 19

PITTSBURGH, PA

[CONTRIBUTION FROM THE MELLON INSTITUTE AND THE SCHOOL OF CHEMISTRY, UNIVERSITY OF PITTSBURGH]

PHTHALIC ACID DERIVATIVES; CONSTITUTION AND COLOR. XVII.[1] TETRABROMO-FLUORESCEIN, TETRABROMO-EOSIN AND SOME OF THEIR DERIVATIVES.

BY DAVID S PRATT, G F HUTCHINSON AND A W HARVEY

Received May 31, 1919

The replacement of hydrogen in the anhydride ring of fluorescein by 4 iodine atoms has been found to alter the equilibrium between the benzenoid and quinoid structure.[2] Whereas fluorescein itself is stable in the latter, or highly colored, modification, the tetra-iodo molecule ordinarily assumes the former arrangement. The present paper deals with certain intermediate bromine derivatives.

Tetrabromo-fluorescein, prepared by condensing tetrabromo-phthalic anhydride with resorcin, shows an equilibrium that lies near the border between the two structural isomeric modifications. The intramolecular forces which determine stability for either form are probably resultants from proximity effects inherent in unsaturated centers residing in the phthalic residue. There is a close relationship throughout the series under investigation existing between these unsaturated centers and the stability of the anhydride ring structure. This structure is encountered only as part of a benzenoid arrangement. When the 4-carbon-1-oxygen ring opens the molecules may rearrange into a quinoid structure with a color change generally, although not necessarily, manifest to the eye. Under other circumstances the ring may open with the formation of a carbinol carboxylic acid but without the marked color change.

The stability of the anhydride ring and benzenoid structure necessarily influences chemical reactivity, as has been noted by various investigators. An example of this may be pointed out in the present instance of salt formation. Tetrabromo-fluorescein with dry ammonia gas gives a diammonium salt where tetrabromo-eosin or octabromo-fluorescein gives a tetrammonium salt. It is felt that a comparative study covering as many cases of these intramolecular resultant effects as possible and including spectrographic data will be of value.

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[1] THIS JOURNAL, 41, 1289 (1919).

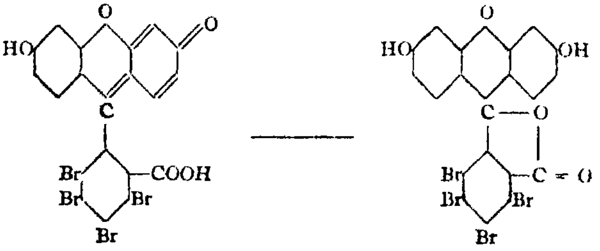
[2] *Ibid.*, 40, 236 (1918).

Tetrabromo-fluorescein.—464 g of tetrabromo-phthalic anhydride were well mixed with 216 g. of colorless resorcin and 216 g. of powdered, freshly fused zinc chloride. Fusion was carried out by gradually raising the temperature during half an hour to 200° with frequent stirring. The color darkened as the melt solidified. Heating was continued for two hours after which the cold fusion was powdered and washed with dil. hydrochloric acid until free from zinc. The crude fluorescein was then dissolved in a minimum of dil. sodium hydroxide solution and precipitated in tall cylinders with vigorous air stirring by adding 2% hydrochloric acid.

The yellow gelatinous hydrate resulting was washed free from chlorides by repeated decantation, filtered off and dried in a water oven. Yield, 90%. Purification was carried out most successfully through the diacetate as it crystallizes well and is readily prepared. Saponification was then carried out by filtering a hot saturated acetone solution of pure diacetate into *5% sodium hydroxide solution and after 72 hours' standing, acidifying* with dilute acid. The product, after drying to constant weight in a water oven, was pure anhydrous tetrabromo-fluorescein. All analyses were made by the modified lime combustion method.

Subs., (I) 0.3239; (II) 0.2827. Cc. 0.1 *N* $AgNO_3$ (I) 19.87, (II) 17.30
Calc. for $C_{20}H_8O_5Br_4$: Br, 49.34 Found (I) 49.03; (II) 48.91

The fluorescein so obtained is a brick-red amorphous powder It changes rapidly to bright yellow when moistened with acetone or ethyl acetate without permanent alteration in weight, behaving in this respect analogously to tetraiodo-fluorescein.[1] This ready transformation from the unstable red quinoid to the stable yellow benzenoid form probably takes place through partial solution of an intermediate loose addition product. The yellow color of benzenoid tetraiodo-fluorescein was attributed to the similar color of tetraiodo-phthalic anhydride from which it is derived, but in this case the parent anhydride is colorless. Heating for a short time at high temperatures reverses the equilibrium with formation of the red form. These changes are represented as



Red. Yellow.

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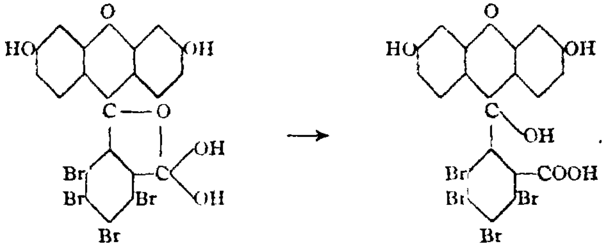
[1] *Ibid.*

The yellow hydrate obtained upon precipitation from alkaline solution was air dried to constant weight at room temperature without visible change in color. Heating at 110° caused a loss in weight corresponding to approximately one molecule of water of constitution, and a partial conversion into the red quinoid form.

Subs., 1.2921. Loss in weight, 0 0318.
Calc. for $C_{20}H_8O_5Br_4.H_2O$: H_2O, 2 70. Found: 2.46.

Alkaline solutions of tetrabromo-fluorescein are deeply colored and highly fluorescent, resembling closely the unhalogenated parent substance. Silk is dyed directly a vivid purplish red similar to that produced by fluorescein. Visual examination, therefore, indicates that the vibrational alterations brought about by the introduction of bromine probably lie chiefly, if not entirely, in the ultraviolet region of the spectrum.

Tetrabromo-fluorescein Carbinol Carboxylic Acid.—When tetrabromo-fluorescein hydrate is treated with absolute alcohol the color changes rapidly to a very much lighter yellow corresponding to the arrangement of the molecule represented by



Hydrous tetrabromo-fluorescein.

Tetrabromo-fluorescein carbinol carboxylic acid.

The resulting carboxylic acid deposits from an alcohol solution in a nearly colorless, amorphous form. Heating at 110° causes a loss in weight corresponding to a molecule of water and a reversion to the yellow benzenoid fluorescein.

Subs., 0.7375. Loss in weight, 0.0173.
Calc. for $C_{20}H_{10}O_6Br_4.H_2O$: H_2O, 2 70. Found: 2 33.

Diammonium Salt.—The salt was formed by exposing a weighed sample of pure anhydrous fluorescein for 18 hours to a current of dry ammonia. When constant weight was attained, the color was bright red. Heating at 100° reconverts the salt into the original fluorescein.

Subs., 0.2520: (I) gain in weight, 0.0123; (II) loss in weight at 100°, 0.0119.
Calc. for $C_{20}H_8O_5Br_4.2NH_3$: NH_3, 4.99. Found: (I) 4.88; (II) 4.72.

Tetrabromo-fluorescein Diacetate.—370 g. of crude tetrabromo-fluorescein was added to 800 cc. of acetic anhydride containing 35 g. of fused sodium acetate. The suspension was heated in a water bath for 30 minutes and finally boiled gently for 20 minutes. The material in suspension gradually lightened until it became nearly colorless. After standing two days, the mixture was poured into water, filtered, washed and dried. The crude diacetate was dissolved in acetone and boiled for several days with successive small portions of bone black. Concentration of the light amber solution gave colorless crystals.

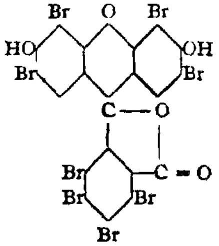
Subs., (I) 0.3964, (II) 0.3156. Cc 0.1 *N* $AgNO_3$ (I) 21.56, (II) 17.10.
Calc. for $C_{24}H_{12}O_7Br_4$ Br, 43.68. Found (I) 43.47, (II) 43.30.

The crystalline diacetate is attacked rather slowly by aqueous alkali. The method of saponification indicated above is preferable as the acetone solution gives flocculent material readily acted upon.

Tetrabromo-eosin.—Anhydrous tetrabromo-fluorescein reacts easily with bromine to give tetrabromo-eosin or octabromo-fluorescein. The replacement of 4 additional hydrogen atoms was carried out by suspending 200 g. of pure tetrabromo-fluorescein in 400 cc. of glacial acetic acid containing 80 cc. of bromine. The mixture was boiled gently for an hour, during which the color lightened to a faint pink. The crystalline material was washed with alcohol and further purified from acetone. A yield representing 80% of pure product was obtained.

Subs., (I) 0.2834; (II) 0.2124. Cc 0.1 *N* $AgNO_3$ (I) 23.48, (II) 17.65.
Calc. for $C_{20}H_4O_5Br_8$. Br, 66.36. Found (I) 66.21, (II) 66.43.

Tetrabromo-eosin shows only a very slight tendency to rearrange into the quinoid or colored form except in the presence of alkali. Its structure should, therefore, be represented as



It is extremely sensitive toward alkali, and is therefore generally obtained faintly tinged with pink. This color is intensified upon heating to 150° but all efforts to shift the equilibrium further towards the red form failed. Tetrabromo-eosin is practically insoluble in alcohol, slightly so in acetone. It dissolves readily in aqueous alkali with a deep red color and slight fluorescence. Such a solution dyes silk an attractive pink.

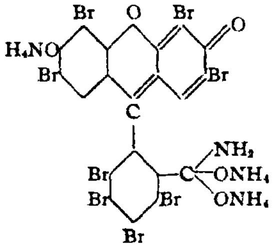
The addition of acid to a dilute alkaline solution precipitated a voluminous pink hydrate which was carefully washed and air dried to constant weight without change in color. Further heating at 110° drove off approximately one molecule of water of constitution.

Subs., 1.3013. Loss in weight, 0.0187.
Calc. for $C_{20}H_4O_5Br_8.H_2O$: H_2O, 1.83. Found: 1.44.

Tetrammonium Salt.—Dry ammonia gas was passed over a weighed quantity of tetrabromo-eosin until constant weight was obtained. The color changed to purple immediately, followed by the formation of a very brilliant deep bronze. The addition corresponded to 4 molecules of ammonia whereas tetrabromo-fluorescein did not react further than the diammonium salt. The ammonia is driven off readily by heating.

Subs., 0.6802. (I) gain in weight, 0.0473; (II) loss in weight at 120°, 0.0468.
Calc. for $C_{20}H_4O_5Br_8.4NH_3$: NH_3, 6.60. Found: (I) 6.50; (II) 6.44.

The addition of 4 molecules of ammonia is probably best accounted for by a rearrangement into the quinoid structure and subsequent direct addition of 2 NH_3 to the carboxyl group. This would give the salt the structure represented by



Tetrabromo-eosin Diacetate.—20 g. of pure tetrabromo-eosin was suspended in 75 cc. of acetic anhydride containing 20 g. of fused sodium acetate. Some of the bright red sodium salt formed at first but upon boiling gently for 30 minutes this largely disappeared. The lumps were then crushed and boiling continued for 15 minutes to insure complete reaction. A theoretical yield of crude product was obtained. The material was recrystallized from benzene until obtained pure as colorless crystals. These contained a molecule of solvent of crystallization as shown by the loss in weight or heating at 130°.

Subs., 1.5622. Loss in weight, 0.0885.
Calc. for $C_{24}H_8O_7Br_8.C_6H_6$: C_6H_6, 6.93. Found: 5.66.
Subs., (I) 0.2520; (II) 0.2500. Cc. 0.1 *N* $AgNO_3$: (I) 19.17; (II) 18.16.
Calc. for $C_{24}H_8O_7Br_8$: Br, 61.06. Found: (I) 60.79; (II) 61.33.

PITTSBURGH, PA.

[CONTRIBUTION FROM THE PHYTOCHEMICAL LABORATORY, BUREAU OF CHEMISTRY, U. S. DEPARTMENT OF AGRICULTURE.]

AN IMPROVED METHOD FOR THE QUANTITATIVE DETERMINATION OF CAFFEINE IN VEGETABLE MATERIAL.

BY FREDERICK B. POWER AND VICTOR K. CHESNUT.

Received June 2, 1919.

The methods that have heretofore been employed for the quantitative determination of caffeine in vegetable products, especially coffee and tea, are exceedingly numerous and varied in character.[1] Several of the older methods have previously been shown to give inaccurate results, which may be attributed to a number of causes. Among these there may be mentioned, in the first instance, the incomplete extraction of the caffeine from the crude material or its partial decomposition by the use of lime in the process of extraction, while a loss of caffeine may also be incurred by the evaporation of large amounts of aqueous extract and the employment of such agents for its purification as lead acetate or animal charcoal. The methods which depend upon the use of an aliquot portion of a chloroform extract of the crude material would also appear to be subject to considerable error through a loss of solvent by volatilization in the operations of filtering and weighing or measuring the liquid, with a consequent alteration of the calculated relations between the latter and the amount of material which it is supposed to represent.

As an investigation undertaken by the authors, which is described in a separate communication,[2] required the determination of caffeine in various kinds of vegetable material, the methods which have heretofore been suggested were subjected to a critical examination. Some of the methods were thus found to be inherently inaccurate, while others are more or less complicated in their manipulative details. It was therefore sought to establish a method which would be both simple and accurate, and which also could be employed, without any considerable modification, for determining the presence or amount of caffeine in material of different physical character.

Although the method to be described embodies some of the features of other methods, the principles and details of procedure, and consequently the results obtained, are so different from most of them as to render it practically new. Nevertheless, we have purposely designated it as an improved method, rather than as a new one The only recorded method with which it may to some extent be compared is that ascribed to Paul and

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[1] Compare Beilstein's *Handbuch d. org. Chem.*, III Auflage, Bd. II, p. 957. Also Ergänzungsband, III, p. 704. Czapek, *Biochemie der Pflanzen*, 1905, Bd. II, p. 244. An especially complete and critical review of methods of assay, in chronological order, is given by Lendrich and Nottbohm, *Z. Nahr. Genussm.*, 17, 241–651 (1909). See also Fendler and Stüber, *Ibid.*, 28, 9–20 (1914).

[2] THIS JOURNAL, 41, 1307 (1919).

Cownley for determining caffeine in tea, which, as given in Allen's *Commercial Organic Analysis*,[1] is essentially as follows:

"Five grams of finely powdered tea are well mixed in a mortar with 2 grams of ignited magnesia,[2] the mixture thoroughly moistened with hot water, again triturated, and then dried at 100°. It is next extracted with boiling alcohol, and the resultant liquid evaporated nearly to dryness. The residue is boiled with 50 cc. of water, and treated with a few drops of dil. sulfuric acid. When cold, the liquid is filtered and repeatedly shaken with chloroform until exhausted. The united chloroform solution is then agitated with a very dilute solution of sodium hydroxide, which removes a little coloring matter, so that on subsequently distilling off the chloroform in a weighed flask the caffeine is obtained perfectly pure and colorless, or at most with a faint green tinge."

A trial of the above-described method for the assay of Maté or Paraguay tea did not give very satisfactory results.

A consideration of the entire subject rendered it evident that the first object to be attained was the complete removal of the caffeine from the crude material, and for this purpose the direct extraction of the latter with hot alcohol appeared to be the best mode of procedure. The elimination from the extract of such plant constituents as are only soluble in water would thus primarily be effected, and whatever may be the form in which the caffeine is contained in the vegetable material, it was ascertained that it could be completely removed by alcohol. It has been assumed by some investigators that in certain drugs the caffeine is partly in the free state and partly in combination, either with tannic acid or, in the case of coffee, as caffeine-potassium chlorogenate, to which the formula $C_{32}H_{36}O_{19}K_2.(C_8H_{10}N_4O_2)_2 + 2H_2O$ has been ascribed.[3] The existence of the latter compound does not appear as yet to have been completely established,[4] and the recorded analyses are not in very close agreement with the accepted formula. The use of lime, magnesia, ammonia, or other alkali in the various methods of assay is evidently with the primary object of liberating the caffeine from its combinations in the drug, but apart from this purpose a weak alkali, such as magnesia, may also serve for removing the tannin or other acidic substances from solution, as in the method of procedure adopted by us. The use of lime is considered objectionable on account of the observation that, under certain conditions, it may cause some decomposition of the caffeine with the formation of ammonia and methylamine, but it has been shown that this is not the case with magnesia.[1]

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[1] 4th edition, Vol. 6, p. 611.

[2] In the original paper by Paul and Cownley, *Pharm. J.*, [3] 18, 417 (1887), to which reference is made in the above-mentioned work by Allen, the authors direct for 5 g. of tea the use of 1 g. of "hydrate of lime," and no mention is there made of magnesia.

[3] Gorter, *Ann.*, 358, 327–348 and 359, 217–244 (1908).

[4] Compare Lendrich and Nottbohm, *Loc. cit.*, p. 264.

Method of Assay.—After a large number of experiments with different kinds of material in order to overcome the various minor difficulties that were experienced, and also to insure the accuracy of the results, the following general method of procedure was finally adopted:

Ten g. of the finely ground material, previously moistened with a little alcohol, is extracted for about 8 hours in a Soxhlet apparatus with hot alcohol. The alcoholic extract is then added to a suspension of 10 g. of heavy magnesium oxide in 100 cc. of water, contained in a porcelain dish, the flask being rinsed with a little hot water, and this liquid added to the mixture. The mixture is allowed to evaporate slowly on a steam-bath or water-bath, with frequent stirring, until all the alcohol is removed and a nearly dry, powdery mass is obtained. This is mixed with sufficient hot water to enable it to be brought on a filter, which preferably should be smooth, and, after thoroughly cleaning the dish by means of a glass rod, to which a piece of rubber tubing is attached, the contents of the filter are washed with successive portions of hot water until about 250 cc. of filtrate is obtained. To the filtrate, contained in a flask of one-liter capacity, is added 10 cc. of a 10% solution of sulfuric acid, which causes the liquid to become much lighter in color, and with some kinds of material, such as *Ilex* leaves, a considerable precipitate is produced. In some cases, as with tea and guarana, it was found necessary to use 20 cc. of the above-mentioned acid in order to prevent the formation of an emulsion on subsequently extracting with chloroform After the addition of the acid, a small funnel is placed in the neck of the flask, and the liquid, which is at first gently heated until any frothing ceases, is kept in a state of active ebullition for half an hour. This treatment is for the purpose of hydrolyzing any saponin that may be present. After being allowed to cool, the liquid is passed through a double moistened filter into a separatory funnel, the flask and filter being washed with small portions of about 0.5% sulfuric acid. The clear acid filtrate is then shaken with 6 successive portions of chloroform of 25 cc. each, which usually separates sharply and quickly, but, if not, can be made to do so by gently rotating the separatory funnel, or, if necessary, by the use of somewhat larger portions of chloroform. The united chloroform extracts are brought into another dry separatory funnel and shaken with 5 cc. of a 1% solution of potassium hydroxide, which serves to remove coloring matter. After complete subsidence of the chloroform solution it is passed through a small, dry filter into an Erlenmeyer flask, the alkaline liquid remaining in the separatory funnel being subsequently washed with two successive portions of chloroform of 10 cc.

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[1] Tassilly, *Bull. soc. chim.*, [3] 17, 596 (1897). Compare also Maly and Andreasch, *Monatsh.*, 4, 369–386 (1883).

each. These washings of the alkali are passed through the previously mentioned filter, and, after washing the latter with a little chloroform, they are added to the first chloroform solution. The chloroform is finally removed by distillation from a water-bath, the residual caffeine brought by means of a little chloroform into a tared beaker, and, after the solvent has been allowed to evaporate spontaneously, the caffeine is dried for half an hour in a water-oven and weighed. On heating for another half hour there is usually a further slight diminution of weight, and this second weighing may be considered to represent the correct amount of caffeine, which, when multiplied by ten, denotes the percentage. As so obtained the caffeine is nearly colorless, and possesses a quite satisfactory degree of purity.

Control Experiments.—In order to ascertain that no caffeine was lost in any of the described operations a number of control experiments were made.

I.—Fifty g. of finely ground coffee was thoroughly extracted in a Soxhlet apparatus with warm alcohol, after which the material was dried on a steam-bath, moistened with 25 cc. of water, and allowed to stand for an hour. It was then extracted for 6 hours in a Soxhlet apparatus with warm chloroform, and the chloroform extract further treated according to the method of Lendrich and Nottbohm,[1] but no trace of caffeine was obtained. It was thus evident that the caffeine had previously been completely removed by extraction with alcohol.

To 50 g. of maté, which in two assays by the above-described method had been found to yield 1.33 and 1.34%, respectively, of caffeine, was added an alcoholic solution of 0.5 g. of anhydrous caffeine, and the whole completely extracted with hot alcohol in a Soxhlet apparatus. This extract was added to a suspension of 25 g. of heavy magnesium oxide in 500 cc. of water, as in the case of all assays when 50 g. of material was used. After evaporating the mixture to dryness, the residue was treated with water, brought on a filter, and washed repeatedly with hot water until about one liter of filtrate was obtained. A portion of the aqueous filtered liquid, representing 10 g. of the original material, was heated with dil. sulfuric acid, again filtered, and extracted with chloroform, when 0.2353 g. of caffeine was obtained. By deducting the amount of added caffeine, corresponding to 0.1 g., the yield of the latter from the maté was 0.1353 g. or 1.35%. This result afforded a further indication that the caffeine originally contained in the drug had been completely removed, and that no loss had occurred in the process of assay.

II.—As the second step in the process consisted in evaporating the alcoholic extract of the drug with a suspension of magnesia, it was deemed important to obtain the assurance that there was no loss of caffeine by adsorption or otherwise during this treatment. It may be considered, however, that in most cases the magnesia would be to a large extent withdrawn from action on the caffeine through its combination with the tannin and other acidic substances of the drug.

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[1] *Loc. cit.*

To 5 g. of heavy magnesium oxide, mixed with 100 cc. of water, was added 0.2084 g. of caffeine, the mixture evaporated to dryness, and subsequently treated as in the described method of assay. The amount of pure caffeine recovered by extraction with chloroform was 0.2045 g. In another experiment 0.2118 g. of caffeine was added to a suspension of 10 g. of magnesia in 100 cc. of water, and the mixture treated as before. The amount of caffeine recovered was 0.2117 g. It will thus be seen that under the prescribed conditions the use of magnesia involves no loss of caffeine.

It was observed in the course of the investigation that somewhat lower yields of caffeine were obtained by the use of light magnesia than with the heavy form, which is evidently due to the more gelatinous character of the mixture formed with the light magnesia, and the greater difficulty of removing the caffeine completely from it by washing. It was also found that the heavy magnesium oxide is of variable character, and some specimens designated as "chemically pure" contained considerable quantities of sodium carbonate. In one sample the amount of sodium carbonate, calculated as anhydrous salt, was 13.9%, and much sulfate and chloride was also present. Other samples contained 7.0 and 8.2%, respectively, of the alkali carbonate.

In order to ascertain whether sodium carbonate in the proportion contained in the most strongly alkaline sample of magnesia caused any decomposition of the caffeine in the process of assay, the following experiment was conducted: Such an amount of anhydrous sodium carbonate as would be contained in 10 g. of the magnesia (1.39 g.) was dissolved in 100 cc. of water, and 0.2003 g. of caffeine added. The solution was then evaporated to dryness, the residue dissolved in water, and the filtered liquid, amounting to 200 cc., extracted with 6 successive portions of chloroform of 25 cc. each. The amount of caffeine recovered, dried at 100°, was 0.1894 g. Although the loss in this instance was not very considerable, it is nevertheless deemed desirable that for the determination of caffeine by the proposed method the magnesium oxide should contain no appreciable amount of sodium carbonate, and it is also particularly important that the heavy form of magnesia be employed.

III.—As one of the essential operations in the proposed method of assay consists in the addition of dil. sulfuric acid to the aqueous liquid obtained by extracting the dry magnesia mixture with water, and maintaining the acid liquid in active ebullition for half an hour, it was considered important to ascertain that no loss of caffeine was thus incurred.

To a solution of 0.2136 g. of caffeine in 200 cc. of water 20 cc. of 10%

sulfuric acid were added, and the liquid kept at the boiling temperature for half an hour. It was then allowed to cool and extracted with 6 successive portions of chloroform of 25 cc. each. The amount of caffeine obtained was 0.2119 g. It was thus evident that no loss of caffeine had been caused by this treatment.

IV.—An experiment was finally conducted for the purpose of determining that no loss of caffeine resulted by shaking its chloroform solution with a dil. alkali.

0.2000 g. of anhydrous caffeine was dissolved in chloroform, and the solution shaken with 5 cc. of a 1% solution of potassium hydroxide. After separating the chloroform the alkaline liquid was washed with two small successive portions of chloroform, the united chloroform solutions passed through a small, dry filter, the solvent removed, and the residual caffeine dried at 100°. The amount of caffeine recovered was 0.1982 g., which indicates that in the process of assay there is no loss of caffeine by the use of alkali for its purification.

The degree of purity of the caffeine obtained by the proposed method of assay was ascertained by nitrogen determinations, using the Kjeldahl method. As a control experiment a specimen of commercial caffeine, designated as U. S. P., was examined.

Subs., 0.1500 g. (anhydrous) gave ammonia equivalent to 30.8 cc. of 0.1 *N* HCl. Found: 0.0431 N or 0.1493 g. caffeine. Purity 99.5%.

The general applicability of the proposed method for the quantitative determination of caffeine has been ascertained by the examination of a number of vegetable products which differed greatly in their physical characters and composition. Although it is not desirable as a rule to employ more than 10 g. of material for the purpose of assay, in some instances 50 g. or even larger amounts were used in order to confirm the accuracy of the results. With such material as the so-called "caffeine-free coffee," which usually contains a very small proportion of caffeine, it is important that at least 20 g. should be used, and 50 g. would be preferable. The value of the method is believed to have been shown by the close concordance of the results obtained in several assays, and even with the larger amounts of material the figures are in remarkably close agreement.

The material examined in the course of this investigation, and the observations pertaining thereto, may be described as follows:

1. *Green Tea.*—A sample of fair quality yielded in two 10 g. assays 1.98 and 2.01%, respectively, of caffeine.

2. *Black Tea* (Oolong).—A sample of ordinary quality yielded in two 10 g. assays 2.43 and 2.44%, respectively, of caffeine. The caffeine obtained from tea was quite white, and evidently of a high degree of purity.

3. *Maté or Paraguay Tea.*—(From species of *Ilex.*) Two 10 g. assays yielded, respectively, 1.44 and 1.46%, and in a 50 g. assay 1.38% was obtained.

4. *Coffee, Roasted Java.*—The yield in a 10 g. assay was 1.22%, and in two 50 g. assays 1.24 and 1.25%.

5. *Coffee, Roasted Rio.*—A 10 g. assay yielded 1.12% and a 50 g. assay 1.07%. From 200 g. of the same coffee 1.10% was obtained.

6. *Coffee, Roasted Santos.*—A 20 g. assay yielded 0.96%.

7. *Coffee, Natural Santos.*—A sample of this coffee was available which consisted of a mixture of (*a*) green and (*b*) dark colored beans. As the latter are rejected in the process of sorting, it was deemed of interest to ascertain the difference in caffeine content of the two kinds of beans.

(*a*) *Green Beans.*—A 20 g. assay yielded 0.97% of perfectly white caffeine.

(*b*) *Dark Colored Beans.*—A 20 g. assay yielded 0.71% of nearly white caffeine.

Although the dark colored beans contain an appreciably smaller proportion of caffeine than the selected ones, they would still appear to possess considerable value for the production of this substance.

8. "*Caffeine-free Coffee.*"—A sample of this preparation, in a 20 g. assay, yielded 0.08% of caffeine, somewhat dark in color.

Through the courtesy of Dr. Walter H. Evans, Chief of Insular Experiment Stations, U. S. Department of Agriculture, and Mr. T. B. McClelland, horticulturist of the Porto Rico Experiment Station at Mayaguez, we have been able to obtain a quantity of coffee leaves and the pulp of the coffee berry. Mr. McClelland has kindly communicated the following information concerning them:

"As the coffee plants are not given much pruning, the amount of leaves as a waste product would be negligible if large quantities were desired. A small amount of leaves could be obtained from November to January, as such pruning as is done is given immediately after the picking of the crop."

"Coffee pulp, immediately after breaking, represents approximately $^1/_3$ of the total weight of the coffee berries as picked. About 5 pounds of coffee berries are required to furnish one pound of market coffee. As the Porto Rican crop varies roughly from thirty million to fifty million pounds, the amount of fresh pulp would run from fifty to eighty million pounds. The water content of this would be very high, and at present it is used only for manuring purposes. It would be available from October to February."

9. (*a*) *Coffee Leaves.*—Several determinations of the amount of caffeine in air-dried leaves gave the following results: Two 10 g. assays yielded, respectively, 0.85 and 0.86%, a 50 g. assay gave 0.85%, and from 100 g. of the leaves 0.82% was obtained. The stems of the plant, separated from the leaves, were likewise examined, but in a 50 g. assay yielded only 0.087%. On extracting a larger portion (about 2 kg.) of the stems with hot alcohol a considerable quantity of a handsome crystalline substance was obtained. This substance, after repeated crystallization from hot alcohol, separated in snow-white, felted needles, much resembling caffeine in appearance, but it gave no reaction for the latter compound by the extremely delicate murexide test, and differed otherwise in its properties. Its more complete examination will be undertaken for the purpose of determining its composition.

9. (*b*) *Coffee Pulp.*—This material, when thoroughly dried, yielded in a 10 g. assay 0.88% and in a 50 g. assay 0.90% of perfectly white caffeine. A preliminary

examination of the other constituents of coffee pulp has shown that they possess chemical interest, and it is intended to pursue their investigation

It may incidentally be noted that in the *National Standard Dispensatory*, third edition, 1916, p. 356, the statement occurs in connection with coffee substitutes that "the pulp of the berry (*sarcocarp*) is practically devoid of caffeine." This is not in accordance with our observations, inasmuch as we have found the pulp to contain such an amount of caffeine as to render its utilization for the production of this substance worthy of consideration, especially in view of the enormous amounts of material available.

10. *Guarana* —In order to obtain as much evidence as possible concerning the general applicability of the proposed method of assay, it was deemed desirable to determine the amount of caffeine in guarana, and for this purpose 10 g of material was employed As previously noted, it was found to be important, as in the case of tea, to heat the aqueous filtrate from the magnesia mixture with 20 cc. of 10% sulfuric acid, in order to effect the hydrolysis of the saponin substances before extracting with chloroform In the latter operation on account of the high percentage of caffeine, 10 portions of chloroform of 25 cc each were employed. The yield of perfectly white caffeine was 4.20%.

For the purpose of comparison a determination of caffeine in the same material was made by the U. S Pharmacopoeia method of assay, when 4.27% of caffeine was obtained. The results by the two methods are therefore seen to be in very close agreement, but the newly proposed method is believed to possess some advantages over that officially adopted. One of these advantages consists in avoiding the use of a definite volume of a filtered chloroform solution, which is assumed to represent a certain proportion of the drug, since an appreciable error may be caused through volatilization of the solvent. There is, furthermore, a more economical use of chloroform, for by the proposed method this solvent is recovered, whereas the Pharmacopoeia directs it to be evaporated, and it is consequently lost.

The results obtained by the examination of the above-described material are summarized in the following table, in which are recorded the yields of caffeine by direct gravimetric determinations and also by the determination of nitrogen in the products.

The leaves of several plants have at various times and in different countries been used as a substitute for tea. An opportunity was afforded us of examining some of these tea substitutes in order to ascertain whether they contain caffeine.

Ehretia macrophylla, Wall. (Fam. *Borraginaceae*).—A small quantity of the leafy twigs of this tropical plant was available through the kindness of Mr. Geo. F. Mitchell, Supervising Tea Examiner of the Treasury Department, who had received it from Adn. Hernandez, Director of Agriculture in the Bureau of Agriculture of the Philippines. This plant is known in the Philippines as "Forest Tea," or by the vernacular name of

Chaa-bundoc. It is stated by Mr. Mitchell that the beverage prepared from it, while not objectionable, has no pronounced or characteristic flavor that would commend it to Americans. No trace of caffeine could be detected in it, and neither the leaves nor the stems of the plant responded to the general tests for an alkaloid.

Name of material.	Percentage yield of caffeine, gravimetric 10 g assay	50 g assay.	Percentage yield of caffeine, calculated from nitrogen. 10 g. assay	50 g. assay.
1. Green Tea	1.98; 2.01	......	1.95	......
2. Black Tea (Oolong)	2.43; 2.44	. ..	2.39	......
3. Maté (Paraguay Tea)	1.44; 1.46	1.38	1.33; 1.35	1.32
4. Coffee, Roasted Java	1.22	1.24; 1.25	1.15	1.16; 1.18
5. Coffee, Roasted Rio	1.12	1.07	1.05	1.00
6. Coffee, Roasted Santos	0.96	..	0.93	..
7. Coffee, Natural Santos:				
(*a*) Green beans	0.97		0.94	..
(*b*) Dark colored beans	0.71	..	0.69	..
8. "Caffeine-free Coffee"	0.08	..	0.06	..
9. Coffee Leaves and Pulp:				
(*a*) Leaves	0.85	0.85	0.77	0.77
(*b*) Pulp	0.88	0.90	0.80	0.85
10. Guarana	4.20	.		.

NOTE.—A 200 g. portion of Rio Coffee yielded 1.10% of caffeine and a 100 g portion of coffee leaves yielded 0.82%

Ceanothus Americanus, Linné (Fam. *Rhamnaceae*).—The leaves of this plant, commonly known as "New Jersey Tea," are said to have been used as a substitute for tea during the American Revolution. A small quantity of the leaves was collected by Dr. R. M. Harper on October 1 in woods near Washington. No caffeine could be found in the leaves, which, however, gave decided general reactions for the presence of an alkaloid.

Psychotria undata, Jacq. (Fam. *Rubiaceae*).—Through the courtesy of Mr. Charles T. Simpson, of Little River, Fla., a small quantity of the leaves and fruit of this plant was collected for us. Inasmuch as it belongs to the same botanical family as that of the coffee plant, and is locally known as "wild coffee," it seemed desirable to consider the possible presence of caffeine, but none of this substance could be found in either the leaves or the fruit.

WASHINGTON, D. C.

[CONTRIBUTION FROM THE PHYTOCHEMICAL LABORATORY, BUREAU OF CHEMISTRY, U. S. DEPARTMENT OF AGRICULTURE.]

ILEX VOMITORIA AS A NATIVE SOURCE OF CAFFEINE.

BY FREDERICK B. POWER AND VICTOR K. CHESNUT.

Received June 2, 1919.

In connection with the war activities of the National Research Council a question was submitted to the Chemistry Committee, of which at the time Lieut. Col. Bogert was chairman, respecting "the possibility of increasing the present production of caffeine, and the utilization of other sources than tea." This problem was referred to one of the present authors, as chairman of the sub-committee on Pharmaceutical Chemistry, for investigation.

The occurrence of caffeine in several distinct families of plants is quite remarkable, and it is also an interesting fact that it is chiefly the plants containing caffeine which have been employed in different countries for beverage purposes. In this connection it may furthermore be noted that the occurrence of caffeine appears to be restricted to certain species of a genus, for it has been stated that a number of species of *Coffea* do not contain it, and the same conditions have previously been observed, and now confirmed by us, with regard to plants belonging to the genus *Ilex*.

The chief source of caffeine, as is well known, is tea, and for its commercial production the inferior qualities, damaged material, and the dust obtained by sifting the leaves are generally employed. Although the so-called *Maté*, *Yerba Maté*, or Paraguay Tea, which is said to be yielded by several South American species of *Ilex*, but is generally referred to *Ilex paraguariensis*, St. Hilaire, contains a notable proportion of caffeine, it appears not to be utilized for the preparation of this substance Nevertheless, according to a report from William C. Downs,[1] commercial attaché at Rio de Janeiro, the amounts of *Yerba Maté* exported from Brazil during the first 6 months of the years 1916 and 1917, presumably for beverage purposes, were, respectively, 40,441 and 24,483 metric tons.

The occurrence of caffeine in the above-mentioned species of *Ilex* suggested a more complete examination of the North American species than had heretofore been made.[2] In an article published by Henry M. Smith,[3] under the title of "Yaupon," the author states that this is "the name given by the Indians to the leaves of *Ilex cassine*, a plant indigenous to the southern states, but found only along the coast from Florida to North Carolina.[4] Mixed with the leaves of other species of the same plant,

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[1] *The Official Bulletin*, Washington, D. C., September 21, 1917, p. 5.

[2] Compare Wehmer, *Die Pflanzenstoffe*, 1911, pp. 456–457.

[3] *Sci. Am.*, March 30, 1872 and *Am. J. Pharm.*, 44, 216 (1872).

[4] According to recent information from Dr. R. M. Harper, the *Ilex vomitoria* is still known locally by different common names. It is commonly called "yupon" in Virginia and northeastern North Carolina and also in Florida and Texas, "yopon" in southern North Carolina, and "cassena" in South Carolina.

Ilex vomitoria and *Ilex dahoon*, it formed 'Cassena,' the basis of their famous 'black drink,' which was used by the red men as a medicine, and as a state drink at some of their religious festivals." The author has also noted that "Yaupon is largely used in the south as a substitute for tea, coffee, and other stimulants; and it is reputed to be very beneficial to inebriates who wish to cure themselves of the love of liquor." The constituents of "Yaupon," as recorded by Smith, such as volatile oil, resin, chlorophyll, gum, etc., render it evident that he employed for his investigation the unaltered leaves of the plant, and not the parched mixture of leaves and twigs to which the name "Yaupon" is also applied. Smith[1] appears to have been the first to have noted the presence of caffeine in a North American species of *Ilex*, and gives the amount found as 0.122%, which was observed to agree very closely with the proportion of 0.13% found by Stenhouse in Paraguay tea. These very low percentages are doubtless to be attributed to imperfect methods of assay, since both kinds of material are now known to contain very much larger amounts of caffeine.

An important contribution to the subject under consideration is a publication by Dr. E. M. Hale,[2] entitled: "*Ilex cassine*,[3] the aboriginal North American tea; its history, distribution, and use among the native North American Indians." After referring to the use of the shrub by our native Indians and by the white people who once adopted it as a beverage, Dr. Hale remarks that "the reason for its disuse is hard to discover, for, in common with the tea and maté, it contains caffeine or a similar alkaloid. The object of this paper is to examine its history, to suggest its restoration to a place among the stimulant beverages, and to inquire into its possible economic value."

In a paper of much interest entitled, "Narcotic plants and stimulants of the ancient Americans," by W. E. Safford,[4] of the Bureau of Plant Industry, U. S. Department of Agriculture, the "black drink" of Florida and the Carolinas has been considered. This is accompanied by an excellent illustration of *Ilex vomitoria* and a reproduction of an old print, dated 1564, showing the black drink ceremony as performed in northern Florida.

In the above-mentioned publication by Hale reference is made to some analyses by F. P. Venable of leaves designated as *Ilex cassine*, which had been recorded at an earlier date.[5] It was stated by Venable that leaves procured from Newbern, N. C., during the winter of 1883 yielded 0.32%

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[1] *Loc cit.*

[2] U. S Dept. Agr., Div. of Bot., *Bull.* 14, 1891.

[3] Much confusion appears to exist with regard to the botanical names of certain species of *Ilex* The *Ilex cassine* of Walter (but not of Linné) is the *Ilex vomitoria*, Aiton, and, as we have shown, it is only the species to which the latter name is now assigned which contains caffeine.

[4] *Annual Report of the Smithsonian Institution*, 1916, p. 416.

[5] Elisha Mitchell, *Sci. Soc.*, 84, II, 85 (1883); THIS JOURNAL, 7, 100 (1885).

of caffeine, and that in the following May leaves obtained from the neighborhood of Wilmington, N. C., were found to contain 0.27% of caffeine.

Experimental.

Through the kind coöperation of Mr. Frederick V. Coville, botanist of the U. S. Department of Agriculture, Bureau of Plant Industry, we have been able to obtain a considerable number of representative samples of *Ilex vomitoria* for the purpose of chemical examination. This material was personally collected during the summer of 1918 by Dr. Roland M. Harper, who, through his previous botanical explorations in the southeastern states, was thoroughly familiar with the plant and the localities where it is most abundant. In the present instance the leaves were collected at various places in the coastal region, extending from Virginia to Texas, and from plants growing under different conditions of soil and climate. In all cases the leaves, stripped from the branches, were sent to us immediately after gathering, and were then dried in the air, without artificial heat. The following enumeration of the different samples of leaves will indicate the localities from which they were obtained, and reference will be made to these numbers in stating their caffeine content.

1. Cedar Island, in Back Bay, Princess Anne Co, Va, (*a*) from plants growing wild, (*b*) from cultivated plants in garden at Munden, Va 2 Smith's Island, at mouth of Cape Fear River, N C 3 About 3 miles north of Georgetown, S C 4. Tybee Island, Ga 5 Coquina hammock, Anastasia Island, Fla 6 Sandy hammock, in central part of Wakulla Co, Fla 7 St George's Island, Franklin Co, Fla 8 Hammocks near Kountze, Hardin Co, Tex, (*a*) young leaves, (*b*) older leaves. 9. Rocky banks of Bee Creek, Travis Co, Tex. 10 Bottoms of Brazos River, Brazoria Co., Tex

In all of the above-mentioned samples the amount of caffeine was quantitatively determined according to the method which has been fully described by us in the preceding paper It may be noted, however, that in the present investigation, for the purpose of control, quantitative determinations of the caffeine were also made with 50 g. of each of the samples, although ordinarily the use of more than 10 g. of material is neither necessary nor advisable. The same method of procedure as that already described[1] was followed, with the exception that for 50 g. of the leaves 25 g. of magnesium oxide was employed, and about one liter of aqueous filtrate was obtained. This was heated with 50 cc. of a 10% solution of sulfuric acid, and, after filtration, the liquid was extracted with 20 successive portions of chloroform of 25 cc. each, the united chloroform extracts being finally shaken with 25 cc. of a 1% solution of potassium hydroxide. The results of the two series of determinations will be seen to be in close agreement, thus indicating the accuracy of the method. This, moreover, has been confirmed by numerous assays of other vegetable material of different character, which are recorded in the preceding publication.

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[1] *Loc. cit.*, p. 1300.

Amounts of Caffeine Found in Different Samples of Leaves.

Number of sample.	Percentage of caffeine. 10 g. assay	50 g. assay.
1(*a*)	1.29; 1.30	1.25
1(*b*)	1.25	1.21
2	0.57	0.54
3	0.95	0.92
4	0.39	0.38
5	0.99, 0.99	0.95
6	0.80	0.78
7	0.40	0.40
8(*a*)	0.95	0.89
8(*b*)	0.32; 0.36, 0.36	0.35
9	1.63; 1.67	1.65
10	0.84, 0.88	0.79

In addition to the above-mentioned collection of leaves of *Ilex vomitoria* we were able to examine two samples of leaves from cultivated plants. These were procured through the kind coöperation of Dr. David Fairchild, of the Bureau of Plant Industry, and they were both definitely identified by Mr. W. E. Safford as the leaves of *Ilex vomitoria*, Aiton. One of these samples, received early in September, was obtained from Glen St. Mary, Fla. Two 10 g. assays yielded 1.38 and 1.42%, respectively, of caffeine, and in a 50 g. assay 1.40% of caffeine was obtained. The other sample of cultivated leaves was received from a nursery at Augusta, Ga., and had been collected in the month of October. It was surprising to find that these leaves were almost completely devoid of caffeine. By the described method of assay 10 g. of the leaves yielded 0.17% of a product which was only partly crystalline. When this was treated with water, and the aqueous liquid evaporated, a color reaction was obtained by the murexide test which was comparable with that produced by 0.1 mg. of caffeine. In view of this anomalous result a sample of leaves was collected in the month of April from the same shrub and again examined. A 10 g. assay of the leaves yielded but 0.16% of a partly crystalline product, which, by comparative color tests, could not have contained more than about 0.5 mg. of pure caffeine Although the amount of caffeine in the designated sample of cultivated leaves was so extremely small that it might easily have been overlooked, the fact of its presence afforded a satisfactory confirmation of the botanical indentification of the leaves as those of *Ilex vomitoria*.

It was deemed desirable, by nitrogen determinations, to ascertain the degree of purity of the caffeine obtained from the leaves of *Ilex vomitoria* although such determinations by the Kjeldahl method had previously

Ilex vomitoria, a shrub of the Southeastern United States, with specimens of caffeine obtained from its leaves. Natural size

been made with the products of assay from a considerable variety of material, and with fairly uniform results.

(*a*) Caffeine from a 50 g. assay of leaves from wild plants, collected near Georgetown, S. C. (No. 3).

Subs., 0.1 g gave ammonia equivalent to 19.1 cc 0.1 *N* HCl, corresponding to 0.0268 N or 0.0928 caffeine. Yield of caffeine. by weight, 0.92%; calc. from N, 0.85%.

(*b*) Caffeine from a 50 g. assay of leaves from cultivated plants, obtained from Glen St. Mary, Fla

Subs., 0.1 g. gave ammonia equivalent to 19.4 cc 0.1 *N* HCl, corresponding to 0.0272 N or 0.0942 caffeine Yield of caffeine by weight, 1.40%, calc from N, 1.32%.

It has already been noted that for the preparation of the so-called "black drink," as in later times for making "yaupon tea," the leaves of *Ilex vomitoria* were first parched before being infused or boiled with water. In order to ascertain whether the caffeine was destroyed by this treatment, a quantity of such material was prepared for us in the accustomed manner by a native of Virginia under the personal observation of Dr. R. M. Harper. The plants used for this purpose were those grown in a garden at Munden, Va., the leaves of which had previously been assayed for caffeine, and are designated in the tabular list as 1 (*b*). As the material consisted of a parched mixture of broken leaves and stems, which had a very unpleasant smoky odor, it was necessary to grind the whole of it in order to obtain a uniform sample for the determination of the caffeine. Fifty g. of the resulting black powder was treated according to the described method of assay, when the yield of slightly yellowish caffeine was 0.5217 g. or 1.04%. Inasmuch as the material examined contained a considerable proportion of the woody stems of the plant, together with the leaves, both of which were in a more or less charred condition, the amount of caffeine found was quite unexpected. In comparing the caffeine content of this material with that of the corresponding sample of leaves (1.21%), it should, however, be considered that it had been very much more highly dried

The result obtained by the examination of the so-called "yaupon" renders it evident that the high temperature to which the material had been exposed had not caused the destruction of the caffeine, and that a beverage prepared from it would possess decided stimulating properties.

In the course of the present work it was deemed important to examine the leaves of all the available American species of *Ilex* for the presence of caffeine, although previous investigators had shown this to be absent in several species, including the European holly, *Ilex aquifolium*, Linné.[1] Samples of leaves of the following species of *Ilex* were therefore obtained, and our thanks are due to Mr. W. E. Safford, of the Bureau of Plant Industry, for their careful botanical identification.

Ilex cassine, Linné, from Little River, Fla.

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[1] Compare Wehmer, *Die Pflanzenstoffe*, 1911, p. 456.

Ilex glabra, Gray, from vicinity of Orlando, Fla.

Ilex laevigata, Gray, from East Hyattsville Swamp, Md.

Ilex myrtifolia, Walter, from plants cultivated at Glen St. Mary, Fla.

Ilex opaca, Aiton, from different localities near Orlando, Fla., and also from vicinity of Hyattsville, Md.

In none of the above-mentioned species of *Ilex* could any trace of caffeine be detected.

Summary.

The results of this investigation have demonstrated that an abundant source of caffeine is available in one of our native plants, namely, *Ilex vomitoria,* Aiton. Although considerable differences in the caffeine content of the leaves of the plant have been found to exist, these are doubtless attributable to varying conditions of soil and climate. It would therefore appear that by the cultivation of the shrub under the most favorable conditions the supply of material for the production of caffeine could be increased to any desired extent.

So far as has at present been ascertained no other North American species of *Ilex* than that above mentioned contains caffeine, and this substance is also not contained in the leaves of the European holly, *Ilex aquifolium,* Linné.

In conclusion the authors desire to express their indebtedness to Mr. Frederick V. Coville, of the Bureau of Plant Industry, for his generous coöperation in securing most of the material for this investigation, and our thanks are also due to Dr. Roland M. Harper, who had so carefully collected the required samples of leaves of *Ilex vomitoria* over a wide range of territory

WASHINGTON, D. C.

NOTE.

Correction.—In the articles on Halogenation XVII and XVIII appearing in the February, 1919 JOURNAL, the following corrections should be made:

P. 287, line 7 of article: for nitrite read nitrile.

P. 288, line 17, read as follows: By the action of bromine on magnesium ethyl iodide, ethyl bromide is obtained.

P. 292: Title of article should read "Direct Iodination."

R. L. DATTA.

78 MANICKTOLA ST.,
CALCUTTA, INDIA.

NEW BOOKS.

Chemistry in Old Philadelphia. 1st Edition. By EDGAR F SMITH, University of Pennsylvania. J. B. Lippincott Company, Philadelphia, 1919 106 pp. 6 figures. 24.5 × 16.5 cm.

The volume is a brief but very interesting and valuable account of the many-sided activities, chemical, literary, and political, of the following men: deNormandie, Benjamin Rush, Priestley, James Woodhouse, Thomas P. Smith, Andrew and Henry Seybert, John Redmond Coxe, Thomas Cooper, W. H. Keating, Gerard Troost, and Joseph Cloud. On account of it, American chemists owe an additional debt to Dr. Smith for the light he has thrown on the development of chemistry in this country. The subject is so interesting that one regrets that the book could not have been expanded and the contributions of the various men somewhat more critically evaluated. We would wish to know more of what Rush himself did, personally or through his students, to carry on the inspiration of Joseph Black.

The work of Priestley in this country is but briefly noted, and must wait for a separate volume such as have detailed for us the work of Hare and Woodhouse. Special attention has been paid to the Seyberts, father and son, for their pioneer work in mineralogy, to Coxe, who was a philosophical rather than a practical chemist; and to Cooper, one of the most interesting figures of the period. In 1790 Priestley wrote a vigorous letter to Joseph Banks, the President of the Royal Society, protesting against the failure to elect Cooper to membership in the Society on account of the radical political views espoused by Cooper. He evidently brought his vigorous political interest with him to this country to which he came in 1793 to see "whether it was a place fit to live in."

It would seem as if too much stress has been laid on deNormandie's analysis of the Bristow Mineral Waters and his application of quantitative methods. While the use of a balance was new in America, in Europe it was not an unusual procedure in water analysis at that time. The credit due to Lavoisier in this connection is not that he was the first to use the balance, but that he was the first to apply it to the general quantitative study of chemical reactions from the standpoint of the conservation of matter; although even in this he had been preceded by Black, whose studies, however, while classic, were brief.

Dr. Smith has cited a partial list of chemical texts which were re-published and oft-times re-edited in America. Most of these were of English origin. There might be added to the list of French works Lavoisier's Chemistry (1806), and Berthollet's "Researches on the Laws of Chemical Affinity," Baltimore, 1809. The author of "Conversations on Chemistry" referred to is Jane (Haldemand) Marcet. The volume appeared in England in 1806, and probably the first American edition was issued from

Sidney's press for Increase Cooke & Company (New Haven, 1809). This had as a frontispiece a picture of the pneumatic cistern at Yale University.[1] John Griscom, the Quaker chemist, was in Geneva, Switzerland, in 1818, and has the following paragraph in his journal: "We afterward called on Dr. Marcet and were introduced to his wife, known as the very sensible and judicious author of the "Conversations on Chemistry," and more recently a work on "Political Economy."

Would it not have been of service, if it had been pointed out somewhat more clearly in this and Dr. Smith's other most valuable volumes, that American Chemistry was not an isolated, independent development, but was simply a phase of the rapid growth that characterized science at that time in England and France. Many of the Americans had received much of their training in Paris, London and Edinburgh, and the discoveries and reports on pure and applied chemistry, for instance, of Dalton, Davy, Gay-Lussac, Thenard, Nicholson, Accum and Ure were as familiar on this side of the Atlantic as on the other. There was constant exchange of knowledge and ideas across the ocean. It is no disparagement to the work in America to realize the close scientific association with the mother country. We must admit, too, that relatively few new things were discovered in America with the exception of Woodhouse's oxyhydrogen blowpipe, and some of Hare's contributions. There was shown, however, by the American chemists an eager desire to comprehend and substantiate the new theories of chemistry, together with a constant effort to repeat the practical experiments about which they had read, to spread the knowledge of chemistry abroad among the people, and to utilize it wherever possible for the further development of technical arts. These aims, although worthy of high praise, were not epoch-making.

This volume can be heartily commended to American chemists, since there are few more interesting topics than the story of how the "Chemical Revolution" influenced the new republic. F. B. DAINS.

Essentials of Modern Chemistry. By CHARLES E DULL. Henry Holt & Co., New York City, 1918. ix + 458 pp. 12 5 X 19 cm $1.40.

This is another text-book intended for secondary schools. In the preface the author says that his aim has been to make the book practical and to show the relation of chemistry to daily life without neglecting the fundamental principles upon which the science is based. He has apparently forgotten that another important ideal to be ever kept in mind is to teach the scientific method of thought while considering the facts and principles of chemistry. The author also calls attention to the fact that the 4 chapters (XII–XV) dealing with the atomic theory, equivalent and molecular weights, valence, and equations have been grouped. To-day there are many chemistry teachers in schools and colleges who believe that the consideration of each chemical theory should be introduced only where it is really needed to explain certain phenomena. Certainly we would prefer not to concentrate our study of these most difficult topics in 4 successive chapters. But the author is undoubtedly on the right track when he discusses the principles of metallurgy by means of a few typical metals, such as iron and aluminum, instead of by a detailed description of a great variety of metals.

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[1] An edition called "The Second American" appeared in Philadelphia the same year containing, in place of the description of the pneumatic cistern of Yale College and a note about Davy's discovery of the alkalies, an "Appendix consisting of a description, with a plate and the manner of using of the new hydro-pneumatic blowpipe invented by Mr. Joseph Cloud, of the mint of the United States."

Will this book stimulate the average boy or girl to study chemistry? This is at least doubtful because, in the first place, it is not written in an attractive style. Its bare concise statements of chemical facts read much like the syllabus of a course in general chemistry. It would require an exceptionally live and enthusiastic teacher to make such a book go. Then, too, its mechanical construction is far below the standard set by our best modern school books. Surely there is little excuse for muddy half-tones, ragged line cuts, and broken type.

On the whole, there does not appear to be much of special interest in the book, although an experienced teacher will find here and there some clever methods of presenting certain difficult topics, such as mixture and compound, catalytic agents, combustion and fire extinguishers, fractional crystallization, ionizing agents, and the replacement series.

N. HENRY BLACK.

ROXBURY LATIN SCHOOL
BOSTON, MASS

The Chemical Analysis of Iron. Eighth edition By ANDREW J. BLAIR. J. B. Lippincott Co, Philadelphia, 1918. 318 pp. 102 figures. 22 5 × 16 cm $5

In general appearance the latest edition of "The Chemical Analysis of Iron" is decidedly attractive. Its binding is good and its paper and typographical work excellent. The drawings for illustration, while not elaborate, are clear and usually show what needs to be known about a laboratory machine, or other laboratory apparatus. Without doubt the above factors have all contributed materially to the book's popularity and somewhat to its usefulness.

But these are not the main reasons why Blair's "Chemical Analysis of Iron" has so strongly appealed to chemists, and especially to the young chemists. To these inexperienced men, the book is especially valuable, offering as it does many practical suggestions on a great variety of subjects, such as laboratory design, apparatus and chemicals. Moreover, the directions for the analytical work are generally given in detail and are frequently supplemented by reasons for the different operations. Again, conditions leading to inaccuracies are discussed. This analytical detail and these discussions while valuable to the beginner are not so valuable to the experienced chemist. It is on this account probably that some chemists in large steel laboratories have dubbed analytical directions in this book "time killers." Sometimes many methods are given for the determination of the same substance. Since an inexperienced chemist cannot always choose wisely it might have been better in the last revision to have eliminated some which are now more or less obsolete and whose main value is historical. On the other hand, the importance of certain subjects, noticeably the electric furnace and its uses in chemical laboratories devoted to iron requires more elaborate treatment.

The value of the book both to the experienced and inexperienced chemist is in no small measure due to the thorough development of the important subject of Alloy Steel Analysis. Everything considered, the book is worth while on the shelves of any chemical library.

FRANK W. DURKEE.

TUFTS COLLEGE

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(Founded by Ira Remsen)

[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY, MCGILL UNIVERSITY.]

THE ESTIMATION OF SULFATES IN A CONCENTRATED ELECTROLYTE AND THE DETERMINATION OF SULFUR IN FOODS.

BY VERNON K. KRIEBLE AND AUTREY W. MANGUM.

Received November 29, 1918

While one of us[1] was engaged in a study of general metabolism in the department of physiological chemistry at the Jefferson Medical College, great difficulty was experienced in the determination of sulfur by the sodium peroxide method in the composite sample of food used. Many of the samples either exploded or caught fire during the oxidation. Our greatest difficulty, however, was due to the fact that we could not get complete precipitation of the barium sulfate. Out of 9 experiments, 7 gave an additional precipitate in the filtrate when it became diluted with wash water, in spite of the fact that the solutions had stood 48 hours after the barium chloride had been added. When the second precipitates were added to the first the totals showed such a wide divergence that it was impossible to tell whether the sulfur balance was positive or negative. It was consequently decided at the suggestion of Professor Hawk to study the problem a little more thoroughly. The present investigation was, therefore, directed to a study of the oxidation of foods by sodium peroxide and the precipitation of sulfates as barium sulfate in solutions containing large amounts of sodium chloride.

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[1] V. K. Krieble and O. Bergeim, in press

The first objective was soon reached in a very satisfactory manner by mixing a suitable quantity of sodium carbonate with the second addition of sodium peroxide in the fusion and subsequently heating just one side of the nickel crucible in order to start the oxidation locally and keep the rest of the mixture in the crucible relatively cool.

The second problem is not an easy one, for it involves the precipitation of barium sulfate in the presence of electrolytes. Many papers have been published on this subject and the general conclusion seems to be that no direct method is satisfactory. This seems especially clear from the recent work of Johnston and Allen,[1] Johnson and Adams,[2] and of Blumenthal and Gurnsey.[3] Johnston and Adams showed that barium sulfate precipitated in a solution containing a large amount of electrolyte had a relatively large amount of foreign substance occluded in the precipitate, and consequently estimation as barium sulfate in such a medium did not give accurate results. They showed, further, that this occlusion was much less if the barium sulfate was precipitated in a solution of high acid concentration. Under such conditions, a certain amount of barium sulfate remained in solution so that the solubility had to be taken into consideration. They got, however, a granular precipitate and very concordant results in fairly strong hydrochloric acid solutions so that a correction could be applied and accurate results obtained. We therefore tried to apply this method to solutions high in sodium chloride such as are obtained in a sodium peroxide fusion.

EXPERIMENTAL.

Materials, Apparatus and Technique.

All the samples of solutions for analysis were measured in either a 10 cc. or a 50 cc. pipet. The same two pipets were used in all the determinations. Either "non-sol" or Jena glass beakers were used. Distilled water was used, which did not give a test for sulfates. Mallinckrodt's C. P. sodium chloride was found to be free from sulfates. When not otherwise stated, precipitation was made with 10 cc. of 10% barium chloride solution without stirring during the addition of the precipitant. The barium chloride was added by means of a calcium chloride drying tube, with a small opening at the bottom which would allow the solution to drop at the rate of about 10 cc. in 4 minutes. If not otherwise stated, the precipitates were washed with 300 cc. of hot water. During ignitions a platinum lid was placed under the Gooch crucible and another one over it. All weighings were made with the Gooch crucible in a glass-stoppered weighing bottle, counterbalanced by another one of about the same size and shape. The results in the tables are all expressed in milligrams.

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[1] J. Johnston, and E. T. Allen, THIS JOURNAL, 32, 588 (1910).

[2] J. Johnston and L. H. Adams, *Ibid.*, 33, 829 (1911).

[3] P. L. Blumenthal and S. C. Guernsey, *Res. Bull.*, 26, Agr. Exp. Sta., Iowa State Coll., 1905.

We used a solution of potassium sulfate as our standard sulfate solution. We had two specimens of the salt, one manufactured by Schuchardt and the other by Baker & Adamson Both were recrystallized several times from water and then thoroughly dried in a hot air oven at 250°. Two solutions were made up and equal amounts analyzed for sulfates, under identical conditions, with the following results:

	$BaSO_4$ Mg
Schuchardt's	248.1, 248.0, 248.0, 248.3, 248.2, 248.1
Baker and Adamson	248.6, 248.7, 247.0

As the two samples agreed we assumed that both were pure.

The asbestos for the Gooch crucibles was prepared in a manner similar to that recommended by Folin.[1] It was placed in a suction flask with equal quantities of water and concentrated hydrochloric acid. Air was drawn through it for several hours. The asbestos was then removed, washed with water and the process repeated. After again washing thoroughly with water the asbestos was placed in the crucibles a little at a time and well packed with a glass rod after each addition. A thickness of about $^1/_6$ of an inch was used.

We first tried the precipitation of sulfates as barium sulfate in the presence of large amounts of hydrochloric acid without any sodium chloride present. 50 cc. of our potassium sulfate solution, equivalent to 251 mg. of barium sulfate, was diluted to 350 cc. with water and 50 cc. of conc. hydrochloric acid. Precipitation was made near the boiling point with 10 cc. of 10% barium chloride solution. The solutions stood 48 hours before filtering.

TABLE I

Precipitation of Barium Sulfate in the Presence of 50 Cc of Conc. Hydrochloric Acid without Sodium Chloride.

Wt. in mg., 249.5, 250.8, 249.8, 250.2, 250.0, 250.8, 250.1, 250.5, 250.0, 250.4, Average, 250.4

This table confirms the view of Johnston and Adams that it is possible to get very concordant results in the presence of high acid concentration. We also found that the precipitate was very granular and easy to manipulate. It is interesting to note that the errors caused by occlusion of potassium sulfate and the solubility of barium sulfate balance each other so that theoretical results are obtained.

The experiments recorded in Table II were carried out in the same way except that 50 g. of pure sodium chloride was added to the solution before the volume was brought up to 350 cc. In Cols. 1 and 2 only 10 cc.

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[1] *J. Biol. Chem.*, 1, 147 (1905).

of the potassium sulfate solution was used, which is equivalent to 50.2 mg. of barium sulfate.

TABLE II.

Precipitation of Barium Sulfate in the Presence of 50 g of Sodium Chloride in 350 cc. of the Solution.

10 cc. of potassium sulfate solution.		50 cc of potassium sulfate solution
2 cc of conc HCl. Mg	10 cc of conc. HCl Mg	50 cc of conc HCl Mg
52.6	51.6	248.0
51.7	50.5	248.3
53.3	.	248.2
52.2	.	248.7
53.5		248.1
..		248.0
.	..	248.1
Average, 52.7	51.1	248.2

This table shows several important facts. First, it confirms the results of former investigators that in the presence of 2 cc. of conc. hydrochloric acid, which is the usual procedure, the weights obtained are invariably too high. Second, it seems to show that very constant results can be obtained even in a very high concentration of sodium chloride. These results were gratifying, as from them it appeared that our chief difficulty had been solved.

We next investigated the solubility of barium sulfate in the filtrate; the occlusion of sodium and potassium sulfate and the occlusion of chlorides in the barium sulfate. We used the method given by Johnston and Allen[1] for determining the solubility of barium sulfate. The results were as follows:

TABLE III.

Solubility of Barium Sulfate in 350 cc containing 50 cc of Conc Hydrochloric Acid.

Without sodium chloride Mg	With 50 g of sodium chloride Mg
6.5	6.9
6.0	5.1
5.3	
6.3	
6.4	
6.1	
Average, 6.1	Average, 6.0

We agree with Johnston and Allen that the solubility of barium sulfate is not appreciably affected by the presence of sodium chloride. Our results are very much lower than their results as they give about 30 mg. for the same volume, but this discrepancy is no doubt explained by the fact that we used a greater excess of barium chloride which would necessarily decrease the solubility of barium sulfate.

The determination of the occlusion of sodium and potassium sulfate in the barium sulfate was also done by a method suggested by Johnston and Allen.[1] The method is briefly as follows: The precipitate is dissolved in conc. sulfuric acid, the solution diluted with a large amount of water, the barium sulfate filtered out, and the filtrate evaporated down and ignited. We added 10% to our actual results, as Johnston and Adams find that only 90% of the occluded sulfate is obtained in one solution and precipitation. The results are given in the following table·

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[1] *Loc. cit.*

TABLE IV

Occlusion of Potassium Sulfate.

Potassium sulfate found Mg	Calc as barium sulfate Mg
8.8	11.8
9.4	12.6
9.8	13.1
Average, 9.3	12.5

The determinations were made on precipitates weighing 500 mg., which were obtained under the same conditions as the results given in Table I. In Table V we have the occlusion in precipitates obtained under the same conditions as those given in Table II, using 50 cc. of conc. hydrochloric acid. These experiments were also made on 500 mg. of barium sulfate.

TABLE V.

Occlusion of Sodium Sulfate.

Calc as sodium sulfate Mg	Calc as barium sulfate Mg
13.7	22.6
13.0	21.3
13.9	22.9
Average, 13.3	22.5

We assumed that the occluded sulfate was sodium sulfate in this series on account of the huge preponderance of sodium in the solution.

The occlusion of chlorides was determined by a method developed by Hulett and Duschak.[2] The ignited barium sulfate is dissolved in conc. sulfuric acid and the hydrochloric acid liberated is extracted with air which then passes through a silver nitrate solution, where the acid is precipitated as silver chloride.

TABLE VI

Occlusion of Chloride.

	Calc as barium chloride	
Wt of barium sulfate used Mg	Without sodium chloride Mg	With 50 g of sodium chloride Mg
251	8.3	9.2
251	9.2	9.2
50		2.8
50		2.6
50	...	3.0

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[1] *Loc. cit.*

[2] G. A. Hulett and L. H. Duschak, *Z. anorg. Chem.*, 40, 196 (1904).

Hulett and Duschak have shown that the amount of occluded chlorides does not increase very much if the barium sulfate is precipitated in the presence of hydrochloric acid, and apparently the presence of large amounts of sodium chloride in addition to hydrochloric acid has very little effect.

It is interesting, though perhaps not very instructive, to calculate the total sulfate obtained, allowing for the solubility of the barium sulfate in the filtrate, the occlusion of the potassium or sodium sulfate, and the occlusion of chlorides.

Johnston and Adams[1] assume that in high acid concentration the potassium sulfate is occluded as potassium hydrogen sulfate and that during the ignition the reaction $2KHSO_4 = H_2SO_4 + K_2SO_4$ takes place. The correction to be applied to bring the occluded potassium sulfate to barium sulfate is, therefore, represented by the formula $2\left(\frac{BaSO_4 \times y}{Na_2SO_4}\right) - y$, where y represents the amount of occluded potassium sulfate as determined by experiment. The above authors have made a slight error in their correction, as they calculate it by the formula $2\left(\frac{BaSO_4 - Na_2SO_4}{Na_2SO_4}\right) \times y$. Our results agree much better, however, if we assume that no sulfuric acid is lost. This is quite possible as the sulfur trioxide may have displaced chlorine in the occluded barium chloride which was present in excess. Unfortunately, we were not able to prove that no sulfuric acid came off during ignition, as we did not have the necessary apparatus. All the determinations in the following two tables were made with a volume of 350 cc. and with 50 cc. of conc. hydrochloric acid. The precipitations were made at temperatures near the boiling point of the solutions. The solutions were filtered 48 hours after precipitation. The calculated weight of barium sulfate for the amount of potassium sulfate used is 251.0 mg.

TABLE VII.
Total Sulfate

	Mg	Mg	Mg	Mg	Mg
Wt. of precipitate . .	250.6	250.8	250.0	250.6	249.8
Corr. for occl. of K_2SO_4 (Av.)	1.6	1.6	1.6	1.6	1.6
Solubility of $BaSO_4$ (Av.) . .	6.1	6.1	6.1	6.1	6.1
	258.3	258.5	257.9	258.3	257.5
Occlusion of $BaCl_2$ (Av.)	8.6	8.6	8.6	8.6	8.6
Total sulfate.........	249.7	249.9	249.3	249.7	248.9

If it is assumed that a molecule of sulfuric acid escaped for every molecule of potassium sulfate remaining in the ignited precipitate, another 6.3 mg. would have to be added to the total.

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[1] *Loc. cit.*

It is rather astonishing that by making the same assumption in regard to the occlusion of the sulfate and chloride very good results are obtained when 50 g. of sodium chloride is present. It is hardly plausible, however, that in this case all the occluded sodium should be present as sulfate or all the occluded chloride as barium chloride.

TABLE VIII

Total Sulfate with 50 g. of Sodium Chloride

	Mg	Mg	Mg	Mg	Mg
Wt. of precipitate	248.1	248.0	248.1	248.0	248.3
Corr. for occl. of Na_2SO_4 (Av.)	4.6	4.6	4.6	4.6	4.6
Solubility of $BaSO_4$ (Av.)	6.0	6.0	6.0	6.0	6.0
	258.7	258.6	258.7	258.6	258.9
Occlusion of $BaCl_2$ (Av.)	9.2	9.2	9.2	9.2	9.2
Total sulfate	249.5	249.4	249.5	249.4	249.7

We, however, were not primarily interested in the mechanism of the precipitation of barium sulfate, but rather a satisfactory method for the estimation of sulfur in food. We therefore tried next to improve the oxidation sufficiently to avoid explosions and fires during the fusion with sodium peroxide. We began our experiments using powdered blood albumen. Two g. of the material was placed in the bottom of a nickel crucible holding about 100 cc. Two cc. of water was added and the mixture stirred with a nickel stirring rod. Five g. of sodium carbonate was then added and the whole well mixed. Sodium peroxide, about 8 g., was now added in small amounts with stirring until the mass became dry and granular. The crucible was then carefully heated with a Barthel alcohol lamp and the mixture constantly stirred until a brown homogeneous fused mass was obtained. Then the lamp was removed and the crucible cooled, after which another 8 g. of sodium peroxide and 2 g. of sodium carbonate were added. The crucible was again heated with the flame pointing at one side of the crucible opposite the inside level of the contents. The object was to get the ignition started locally without getting the whole crucible and contents warmer than necessary. After the ignition started, the lamp was quickly removed and the crucible covered with a lid. Usually the reaction continued until all the contents were fused but sometimes more heat had to be applied. After the mass had thoroughly fused, the lamp was put under the crucible and the heating continued for 10 minutes, during which the crucible was turned from side to side in order to make sure that all the fragments adhering to the sides were thoroughly oxidized. After the crucible and contents were cool, they were placed in a beaker containing about 100 cc. of water, and placed on a hot plate and digested until all the material was dissolved. The crucible was removed and washed, and the wash water run into the beaker. The solution was then carefully neutralized with conc. hydrochloric acid, and the desired amount of excess hydrochloric acid added. This method worked fairly well on blood albumen—about one explosion in 4 fusions—but was quite unsatisfactory with composite food samples having an average amount of fat. One of these samples was made up of 2 parts of milk, 2 of meat, 2 of corn flakes, one of egg yolk and 4 of soda biscuit. The second sample was the same as the first, except that potato chips were substituted for the egg yolk. The ingredients, however, came from a different source. The materials had all been dried at 110° before they were mixed. In these experiments the explosions were much more numerous. We, therefore, increased the amount of sodium peroxide to 26 g. and the sodium carbonate to 8 g. The procedure remained the same until the first heating was completed, then instead of adding about 8 g. of sodium peroxide enough was always added to bring the total for each oxidation to 26 g. After this 3 g. of sodium carbonate instead of 2 was added and mixed with the peroxide. The second heating was then carried out as before, *i. e.*, by starting the ignition at one point instead of heating the whole crucible. We found that this method is quite satisfactory for from 2 to 3 g. of organic material It was tried on some 50 samples of oats, hay and straw without a single fire or explosion. With composite food samples it was very nearly as successful, the loss being one in 10 to 12 fusions. The method was submitted to one of the American Agricultural Experiment Stations, where it has been used with success for some time.

TABLE IX

Analyses of Organic Materials

Blood Albumen.

Mg. $BaSO_4$ Excess conc. HCl 2 cc	Mg. $BaSO_4$ 50 cc
163.2	157.2
161.4	155.8
166.9	155.2
Composite Food I	
...	38.3
...	39.2
...	39.6
...	39.7
Composite Food II	
47.6	19.5
48.0	14.9
37.5	21.1
46.8	21.4
49.6	35.3
44.5	33.5
42.4	34.3
49.5	34.0
50.6	...
44.5	...
52.0	...

The clear solutions obtained from the above fusions by neutralization and filtration were diluted with water to a volume of 350 cc. after adding the stated amount of hydrochloric acid. 10 cc. of 10% barium chloride solution was added when the temperature was near the boiling point and the solutions were allowed to stand for 48 hours before filtering.

Until the results given in Table IX were obtained, it was thought that precipitation made in high acid concentration would insure complete precipitation of barium sulfate in the presence of a large amount of sodium chloride. The filtrates from the first 4 determinations given in the above table under Composite Food II with 50 cc. of conc. hydrochloric acid contained barium sulfate after they had stood for several days. The same was true of many determinations with 2 cc. of conc. hydrochloric acid. Apparently small amounts of sulfate are not completely nor uniformly precipitated in a conc. hydrochloric acid and sodium chloride solution, although precipitation seems to be complete under the same conditions when the amount of sulfate is much larger. To make sure that this incomplete precipitation was not due to something present in either the chemicals used or the food itself which might act as an anticatalyst, we performed a series of experiments with pure sodium chloride and potassium sulfate. The experiments were carried out under the same conditions as those of Table II, except that we used 10 cc. of our potassium sulfate solution, which is equivalent to 50.2 mg. of barium sulfate. The results are given in the following table·

TABLE X

Precipitation of Small Amounts of Barium Sulfate in the Presence of 50 g of NaCl, and 50 cc of conc HCl, in 350 cc.

Mg. $BaSO_4$.	
46 7	48 1
45 1	46 1
36 6	37 6
37 6.	42 4
44 3	

It is quite evident from these results that the incomplete precipitations noted in Table IX were not due to any substance in the food As we had such excellent results with larger amounts of sulfate present, it was considered possible that better results might be obtained by slightly changing the conditions under which the precipitation was made.

In Table XI are given the results obtained by adding the barium chloride at various temperatures. In the last 3 determinations the solutions were kept near the boiling point on the hot plate for at least 5 hours after the barium chloride was added. All the experiments were made in the presence of 50 g. of sodium chloride and 50 cc. of conc. hydrochloric acid. All the solutions stood 48 hours before filtering.

TABLE XI.

Temperature Effect on Barium Sulfate Precipitation.

Volume. Cc.	Temperature. Degrees.	Barium sulfate found. Mg.
500	23	34.4
500	23	29.8
500	23	32.5
350	80	39.1
350	80	40.1
350	80	40.0
350	b. p.	46.7
350	b. p.	46.1
350	b. p.	45.8
350	b. p.	51.6
350	b. p.	50.5
350	b. p.	42.4
350	b. p.	44.3
350	Precipitated near b. p., stood 96 hrs.	47.3
350	Precipitated near b. p., stood 96 hrs.	46.1
350	Precipitated near b. p., stood 96 hrs.	47.6
350	Precipitated at b. p. and heated 5 hrs.	17.6
350	Precipitated at b. p. and heated 5 hrs.	27.6
350	Precipitated at b. p. and heated 5 hrs.	37.2
	Calc	50.2

The above determinations indicate that the best results are obtained when the barium chloride is added at the boiling point of the solution, but that even at this temperature precipitation is not always complete. No great advantage is gained by letting the solutions stand an extra 24 hours. Since most of the barium sulfate is precipitated in those experiments where the barium chloride was added at the boiling point, it is astonishing that keeping the solutions at this temperature for several hours and then allowing them to stand for some 40 hours at the room temperature gives such poor results.

In a few experiments the solution was stirred for 3 hours after the barium chloride was added and then allowed to stand for 48 hours, but no great advantage is gained by this procedure. The quantities used were the same as in the last table. The barium chloride, however, was added at the room temperature. The results on two experiments were 41.6 and 42.6 mg., respectively.

Having found no conditions under which complete precipitation of small amounts of sulfate in the presence of large amounts of sodium chloride could always be obtained, it was decided to resort to an evaporation method. Johnston and Adams[1] have stated that evaporation immediately after precipitation will give satisfactory results. This, no doubt, is true under all ordinary circumstances, but it apparently does not hold in a concentrated electrolyte, according to our results in Table

[1] *Loc. cit.*

XII. Precipitation was made near the boiling point in a volume of 350 cc. containing 50 g. of sodium chloride and 50 cc. of conc. hydrochloric acid. The evaporations were made immediately on a hot plate in Jena glass beakers.

Table XII

Method of Evaporation of Johnston and Adams

$BaSO_4$: 266.2, 252.5, 262.8, 250.2, 252.2 mg. Calc., 251.

In the next series of experiments the solutions were allowed to stand for 48 hours after the barium chloride was added before they were evaporated. The other conditions were the same as in the above series except that the amount of potassium sulfate used was cut to one-fifth.

Table XIII

Method of Evaporation

Evaporation after filtering $BaSO_4$ Mg	Evaporation without filtering $BaSO_4$ Mg
53.6	55.7
54.9	55.6
	54.7
	54.4
	56.2
	54.8
	54.5
	54.1

Calc., 50.2

In a few cases the barium sulfate was filtered out at the end of 48 hours before the solution was evaporated. The residue from the evaporation was then taken up in water slightly acidulated with hydrochloric acid and filtered through the same filter paper. This extra manipulation, however, is not justified as the results are about the same as those obtained without filtering. All the results are a few mg. too high, but they are sufficiently consistent that a correction can be applied. We feel that results obtained by this method are far more satisfactory than those obtained by the usual procedure. We analyzed composite food II again using the above method, and obtained 47.7, 48.4 and 46.2 mg. of barium sulfate after correcting for the occlusion.

Our Proposed Modification of the Sodium Peroxide Method.

We propose that the determination be carried out in the following way: A suitable quantity (2–3 g.) of the organic material is placed in a nickel crucible which holds about 100 cc. From 2 to 3 cc. of water is added and the mixture well stirred with a nickel stirring rod. 5 g. of sodium carbonate is then added and the whole well mixed. Sodium peroxide is now added in small lots, stirring after each addition until the whole mass becomes dry and granular. The crucible and contents are then carefully heated with a Barthel alcohol lamp until the mixture becomes a homogeneous well-browned fused mass, stirring being continued during the heating. The crucible is then partly cooled and enough sodium peroxide added to make a total of 25–26 g. 3 g. of sodium carbonate is also added and mixed with the peroxide. The crucible is then heated by pointing the flame at a position opposite the level of the contents until the first signs appear that the oxidation has started, when the flame is removed and the lid placed on top of the crucible. When this first ignition does not melt the contents completely, the heating must be continued in a similar way. The heating is usually continued for 10 minutes after the mass is thoroughly fused. During this heating the crucible is inclined from side to side to insure that all the material sticking to the walls is thoroughly oxidized. After the crucible is cool it is put into a large beaker containing about 100 cc. of water, placed on a hot plate, and digested until the contents are all dissolved. The crucible is then washed and removed and the solution neutralized with conc. hydrochloric acid and filtered if necessary. 50 cc. of conc. hydrochloric acid is now added and the solution brought to a volume of 350 cc. The solution is brought to boiling, then removed from the hot plate and precipitation made with 10 cc. of 10% barium chloride solution, added by means of a dropper, at the rate of 10 cc. in about 4 minutes. After standing for 48 hours, the solution is evaporated to dryness on a hot plate and the precipitate taken up with water. One to two cc. of conc. hydrochloric acid is added. After standing for about 18 hours the precipitate is collected in a Gooch crucible, washed, dried, ignited to constant weight, and weighed in the manner which has already been given in this paper.

The results obtained by the method will be high. A correction should be applied, derived from a comparison of the amount of barium sulfate obtained by making a determination on a solution of sodium or potassium sulfate with the calculated amount. This solution should be of such strength that the amount taken should give about the same amount of barium sulfate as obtained from the food. The analysis of this synthetic solution should be made in exactly the same manner as the analysis of the sample of food. It is obvious that if the amount of silica is appreciable it must be removed in the usual manner before precipitation is made.

This method is long and rather tedious and we do not propose that it should be used indiscriminately. Of many substances in which the sulfur content is relatively high, a suitable quantity can be oxidized with much less peroxide and consequently an evaporation may not be necessary to precipitate all the barium sulfate. But we do believe that when the sulfur content of the material is low and when difficulties from fires and explosions are encountered, our modification is a decided improvement both in the oxidation process and in the final estimation of sulfates.

MONTREAL, CANADA

[CONTRIBUTION FROM THE SEVERANCE CHEMICAL LABORATORY OF OBERLIN COLLEGE.]

THE VIBRATION AND SYNERESIS OF SILICIC ACID GELS.

BY HARRY N. HOLMES, WILFORD E KAUFMANN AND HENRY O. NICHOLAS.

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In earlier work with silicic acid gels one of us noticed a sound-producing vibration when the vessel containing a certain gel was lightly tapped. Kohlrausch[1] and Hatschek[2] made similar observations, but did not investigate the phenomenon. Evidently it was not very striking. W. E. Henderson[3] secured some vibration with a ferrous hydroxide gel.

We planned a study of the conditions affecting vibration frequency of the gel hoping to throw some light on the structure of gels, and the cause of the vibration.

The Pitch of Vibration.

A "water white" sodium silicate solution was poured into an equal volume of acid and the mixture allowed to set to a solid gel. The water glass used was free from iron and was found, by analysis, to be 1 Na_2O :-3 27 SiO_2. When diluted to a specific gravity of 1.06 it was neutralized by an equal volume of 0.54 N acid, using phenolphthalein as an indicator. The time of "set" varied from minutes to weeks depending on concentrations and other factors. All tubes of gels were corked to prevent drying.

Preliminary experiments with ordinary test-tubes indicated that an excellent mixture for vibration study was made by adding water glass of 1 15 sp gr. to an equal volume of 6 N hydrochloric acid. This set to a solid gel in about one hour and reached its highest vibration frequency in about two days.

Before any exact measurements of pitch could be made it was necessary to standardize such conditions as diameter and length of tube. It was found that gels in tubes 8 mm. in diameter cracked badly in 3 days even though the tubes were corked. Gels in 14 mm. tubes did not crack in two weeks, this difference of behavior being probably due to the deeper meniscus in narrow tubes. We found that above a certain minimum length of gel column for each tube the pitch did not change with increase in length. In a 155 mm. test-tube this minimum length was 40 mm. With this exception extra length of tube above the gel had no effect. Tubes of wood, brass, porcelain, etc., were tried and were also found to allow vibration, but the advantage of convenience lay with glass tubes.

We finally decided to use ordinary test-tubes 150 × 17 mm. The volume of the gel mixture in each experiment was 20 cc., more than half filling the tube. When we came to measure the exact pitch of the vibrating gels other difficulties were experienced. The quality of sound produced on tapping the tubes of gel was so different from the tone of a piano, siren or sonometer that we were unable to get accurate comparisons. Recourse was had to an old music box in which the sound was produced when metallic teeth of different length were struck on a revolving cylinder. This keyboard was readily calibrated as to the exact vibration frequency of each tooth, and produced a tone sufficiently similar in quality to that of the vibrating gels. Tuning forks would have served, but were inconvenient.

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[1] *Z. phys. Chem.*, **12**, 773 (1893).

[2] *Introduction to the Physics and Chemistry of Colloids*, Blakistons, 1916, 2nd edition, page 55.

[3] Private communication.

As stated above, the pitch did not vary with the length of the gel column. For example, gel columns 60 mm., 90 mm. and 120 mm. in length, but of equal diameter, vibrated, on tapping, with a frequency of 1024 per second, two octaves above middle C, indicating that the vibrations are not longitudinal. We then prepared columns of equal length but different diameters. The vibration frequency of the column 34 mm. in diameter was 341 per second; of the column 23 mm. in diameter, 640 per second; of the column 15 mm. in diameter, 1152 per second. Evidently the vibration frequency varies approximately inversely as the diameter, and consequently the vibrations are transverse.

We found that the pitch rose with increase in the concentration of the silicic acid formed. This is shown in Fig. 1, which is given in two parts for clearness. The abscissa represents the density of water glass solution which was mixed with an equal volume of 4 *N* acid. Since the water glass of 1.06 density is neutralized by an equal volume of 0.54 *N* acid the excess of hydrochloric or other acid used can be determined by subtracting the appropriate values from 4 *N*. As there was more than enough

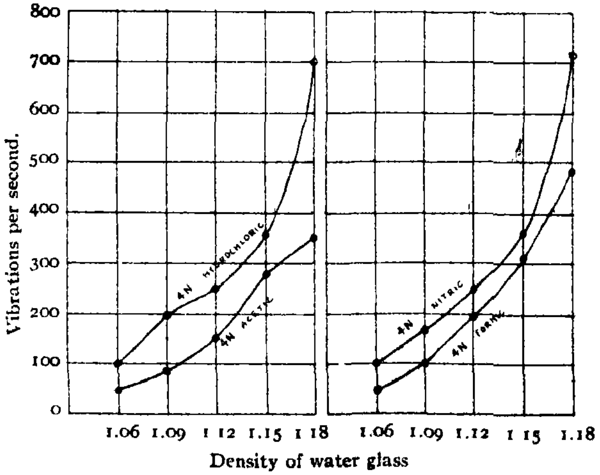

Fig. 1.—Relation of Silicic Acid Concentration to Vibration Frequency.

acid added to release all the silicic acid the curves actually represent the pitch corresponding to different concentrations of silicic acid.

It is important to note that the pitch is higher with gels made by the use of the more highly ionized acids. This fact led us to study the effect of excess hydrogen-ion concentration on a definite concentration of silicic acid. We added to water glass of 1.12 sp. gr. more than enough acid to react completely with the sodium silicate. Six samples were taken and 6 different acids used. In all experiments the actual amounts of silicic acid liberated were the same. Fig. 2 shows curves for gels involving the use of 3 organic and 3 mineral acids.

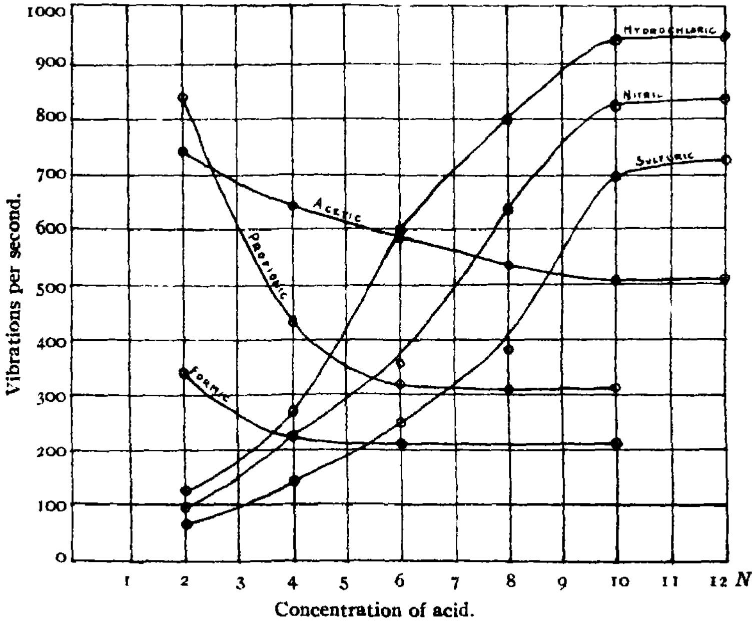

Fig. 2.—Relation of Excess Acid to Pitch of Vibration.

It is evident that the pitch rises with increase in concentration of hydrogen ion, up to a certain point, in the case of gels made by mineral acids. The pitch of sulfuric acid gels is lower at all corresponding points than that of gels made with the more highly ionized hydrochloric or nitric acids. A startling contrast is found in the behavior of gels made with organic acids. With increase in excess of acetic, propionic or formic acids the pitch falls. It is true, of course, that the sodium acetate formed in the reaction of sodium silicate with acetic acid represses the ionization of the acetic acid excess so that the hydrogen-ion concentration is less than with similar gels made with the stronger acids. This, however, does not account for the marked differences shown in Fig. 2. The repression of ionization of the weak organic acids is relatively greater with a small excess of the acid than with the gels containing a greater excess. Hence the hydrogen-ion concentration steadily increases with increase in excess of added acid. Pitch, then, does not always rise with increase in hydrogen-ion concentration.

There is, of course, an increase in the concentration of acetic acid molecules, for example, and these molecules must have a marked influence on the structure of the gel and hence on its pitch. The concentration of molecules of hydrochloric and the other strong acids is low, due to their greater ionization.

Basic gels made by mixing water glass with an amount of acid insufficient to react with all the sodium silicate vibrate with very low frequency. Neutral gels, setting almost instantly, are rather soft and vibrate with still lower frequency than the basic gels.

Rigidity of gel structure is unquestionably the main factor in sound production. Gels in thick walled tubes ring with higher pitch than gel columns of equal diameter in thin walled tubes. The total diameter of gel plus glass is greater in one case but the effect of greater rigidity of glass outweighs the effect of greater diameter.

Syneresis.

By syneresis[1] is meant the separation of water solutions from highly hydrated substances such as silicic acid gels. The breaking of custards into solid and liquid on overheating and the formation of curds and whey from milk are common examples. This phenomenon is almost universal. The subject of syneresis was introduced by an attempt to explain the vibration of certain gels. We knew that the gels vibrated as rigid solids on being struck but we also felt that they were under tension in an effort to contract. To prove this we sought to line the test-tube with some surface to which the gels could not adhere. Then if there was any tendency to contract, the gels could pull away from the walls because free to do so. The glass was coated with vaseline, paraffin, camphor, sulfur, collodion, etc., but of these vaseline was by far the best. It was melted and poured around until, on cooling, a rather thick layer formed. Gels formed in vaselined tubes contracted freely to a much smaller volume and not by mere evaporation, as the tubes were corked. A paper-thin glass bulb was filled with the gel mixture and on setting the gel contracted so powerfully that the glass caved in. In this experiment the glass was not vaselined so that the gel adhered strongly to it. Contraction was thus clearly shown, and naturally it follows that gels in glass tubes not vaselined must be under considerable tension as long as the gel adheres to the glass.

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[1] Capillary-held water is not properly included in the term "Syneresis"

But to prove that tension influenced the pitch of the vibrating gel was another matter.

The same gel mixture (water glass of 1.15 sp. gr. and 6 *N* nitric acid) was poured into a plain test-tube and also into a vaselined tube of the same diameter. On standing 8–10 days the gel in the vaselined tube had contracted so much that it could be shaken out. On tapping this gel thus removed from the tube it was found to vibrate just as did the gel under tension in the plain tube. But the vibration frequency of the gel in the tube was 1024 with a diameter of 20 mm. while the free gel had contracted to a diameter of 16.6 mm., and vibrated only 768 times per second. Since pitch varies in a general way inversely as diameter, the free gel might have been expected to yield a higher pitch, especially since its density was greater. The fact that its pitch was lower is proof positive of the importance of tension in sound production, for the greater the tension the greater the rigidity. Slight syneresis (separation of water solution) was common as gels stood, increasing with time, and when gels split syneresis became considerable. Marked syneresis quickly developed when gels stood in vaselined tubes A gel free to contract simply squeezed out a volume of liquid equal to the decrease in volume of the gel.

To study the effect of external surface 4 bulbs, lined with vaseline, were filled with gel mixture and allowed to synerize.

TABLE I —EXTENT OF SYNERESIS

Volume of gel in cc.	Syneresis, volume of solution in cc	Syneresis in cc to 1 cc of gel	Surface of spheres in sq cm
35	4 90	0 114	52.5
90	9 72	0 108	81.0
250	25 75	0.103	210 0
1140	87 8	0 077	285.0

Table I shows that syneresis is relatively much greater in small spheres than in the larger spheres. The phrase "specific syneresis" might be applied here. The relation of surface to volume of spheres increases rapidly as the volume of the sphere becomes small, in fact, the syneresis of spherical gels closely parallels the change in the relation of surface to volume. This is excellent proof that syneresis varies directly as the free surface. To test this theory further we poured equal volumes of gel mixture (50 cc.) into vaselined vessels such that one gel was 70 mm. wide and 15 mm. deep; a second gel, 50 mm. wide and 28 mm. deep; a third, 40 mm. wide and 40 mm. deep; and a fourth, in a narrow tube was 25 mm. wide and 125 mm. deep. The syneresis of the first was 6.6 cc., of the second 6.3 cc., of the third 5.18 cc., and of the fourth 9.2 cc. The fourth had the greatest free surface and consequently the greatest syneresis. The third had the least surface, being nearest to spherical in shape, and had the least syneresis.

We also found that increase in free surface due to cutting gashes in a gel increased the syneresis. A cube of a newly set gel was cut out from a larger mass and placed in a stoppered vessel. It synerized as great a volume of liquid as an equal volume of the same gel in a vaselined tube and 7 times as much as in an unlined tube.

The time element was very important. Syneresis began sooner with some types of gel than with others and continued for months, although at a decreasing rate. Silicic acid gels made with hydrochloric acid were slower to pull away from vaselined tubes. Out of a series of 120 tubes only 3 had completely pulled away from the vaseline in one month. Gels made with nitric and sulfuric acids pulled away in 8 to 10 days; gels made with acetic, formic or propionic acids in 10 to 15 days. The contraction was more rapid with gels of higher silicic acid concentration.

TABLE II.

Relation of Syneresis to Concentration of Silicic Acid.

Volume of Gel, 20 cc. Equal Volumes of 10 *N* Formic Acid and Water Glass.

Sp. gr. of water glass	Syneresis, cc. of solution
1.09	3.5
1.12	4.7
1.15	5.2
1.18	5.8

In Table II the 10 *N* formic acid was more than enough to react with all the sodium silicate so the variation in density of water glass used corresponds to a similar variation in the concentration of silicic acid formed. Similar results were obtained using 4 *N* acetic acid and 10 *N* nitric acid. With hydrochloric acid syneresis was inconveniently slow.

TABLE III.

Relation of Syneresis to Excess of Propionic Acid.

Volume of Gel, 20 cc. Equal Volumes of Propionic Acid and Water Glass of 1.12 Sp. Gr. Used.

Normality of propionic acid.	Syneresis, cc. of solution
2	5.4
4	2.9
6	2.7
8	2.3

Water glass of 1.12 sp. gr. required an equal volume of *N* acid to neutralize it, so the gels made as in Table III contained the same concentration of silicic acid. With increase in the excess of propionic acid syneresis decreased. Similar results were obtained by the use of citric and formic acids. Very different results were obtained using nitric acid. With increase in the excess of nitric (or other mineral acid) syneresis increased.

This difference accords well with the different effects of organic and mineral acids on the pitch of vibration. The depressing effect on both pitch and syneresis exerted by organic acids can be due only to the molecules of the acid. Were it merely a function of hydrogen-ion concentration trichloroacetic acid should produce gels of higher pitch and greater syneresis than gels from the less ionized acetic acid. Such was not the case.

TABLE IV.

10 cc. of Water Glass (1.15 Sp. Gr.) Mixed with 10 cc. of 3 *N* Acid. Time, 2 Weeks.

Acid	Vibration frequency.	Syneresis, in cc. of solution.
Acetic	682	4.7
Monochloroacetic	427	4.4
Trichloroacetic	320	2.2

It is clear from Table IV that un-ionized molecules of trichloroacetic acid have a greater influence on the rigidity and contraction of silicic acid gels than have the un-ionized molecules of acetic acid.

The neutral gels studied gave but little syneresis. Interesting results were obtained with basic gels. Very basic gels set with extreme slowness and were unsuitable. On setting they do not "bind" all the water but coagulate as a soft layer. Moderately basic gels set in solid form and then separate very large volumes of water solution. After standing two months a gel made from 10 cc. of water glass of 1.18 sp. gr. and 10 cc. of *N* acetic acid separated 18 cc. of solution, the gel having contracted to a volume of 2 cc. This was not a case of drying out for the shriveled gel was immersed in the solution. As in all experiments, the tube was corked.

Many other gels could be studied with respect to pitch and syneresis. For example, a gel made with equal volumes of water glass, of 1.15 sp. gr., and 3 *N* citric acid had a vibration frequency of 1024, two octaves above middle C. A very slightly basic gel of this type made with water glass of 1.12 sp. gr. and 0.8 *N* citric acid showed marked syneresis. Neutral gels in general had very low vibration frequency.

A very beautiful tone was produced from a heavy-walled pint milk-bottle half full of a gel made with water glass of 1.15 sp. gr. and 6 *N* hydrochloric acid. On holding this bottle lightly by the top and swinging it sharply against a wooden table, or similar object, overtones could be detected. The water (of syneresis) on the surface was thrown into a wave pattern and drops splashed against the stopper.

Summary.

1. Vibrating silicic acid gels were made which on tapping produced a tone two octaves above middle C.

2. Such gels vibrate as rigid solids, but tension is an important factor. That they are under considerable tension is proved by their great contraction in vaselined tubes.

3. Contracted gels removed from vaselined tubes have a lower vibration frequency than similar gels adhering to the walls of tubes of equal

diameters. Since vibration frequency varies inversely as the diameter of gel column, tension must exert some influence on pitch.

4. Vibration frequency varies directly as the concentration of silicic acid, increases with excess of mineral acids, but decreases with excess of organic acids.

5. Syneresis increases with increases in concentration of silicic acid, increases with excess of mineral acids, and decreases with excess of organic acids. For acid gels the same factors that increase vibration frequency (by increasing tension and thus effective rigidity) also increase syneresis. Vibration and syneresis have a direct relation to tension. Basic gels are somewhat abnormal in this respect.

6. Syneresis (separation of water solution from gels) varies directly as the free surface. When gels contract in vaselined tubes far more liquid separates than from equal volumes of gel in plain tubes to which the gel adheres.

7. The extreme in syneresis was observed with moderately basic gels. The solution synerized was as much as 90% of the volume of the gel in some instances.

OBERLIN, OHIO

THE VAPOR PRESSURE OF TETRANITRO-METHANE.[1]

BY ALAN W C MENZIES

Received June 17, 1917

The measurements in a portion of the range here reported were made in 1918 at the request of the Division of Chemistry and Chemical Technology of the National Research Council, and were desired for purposes connected with the war. Because such data have a permanent value, however, it was thought desirable to extend the measurements over a considerably wider range than was called for at that time.

The sample of tetranitro-methane furnished for the work, about two cc., was somewhat small for effective purification by fractionation. Its boiling point was found to be 125 7° under 760 mm. pressure, however, which is in close agreement with the reported values of Schischkow[2] and of Chattaway,[3] both of whom, from independent observations, obtained 126° as the normal boiling point. Berger[4] states that the boiling point of his, apparently less homogeneous, preparation was 124–125° under 750 mm. pressure; and this corresponds to temperatures 0 4° higher at 760 mm. In spite of this concordance in boiling point, the possibility of impurity remains the chief uncertainty in the data here recorded; and it is therefore superfluous to elaborate details of the measurements.

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[1] N. R C War Problem No 142

[2] *Ann.*, 119, 248 (1861)

[3] *J. Chem. Soc*, 97, 2099 (1910)

[4] *Bull. soc. chim.*, [4] 9, 26 (1911).

A modified form of the static isoteniscope method was used, with the precautions and corrections previously described.[1] The thermometry was in agreement to 0.1° with the 1914 scale of the Reichsanstalt. Chattaway and Berger both report slight decomposition at the boiling point. The behavior of the sample studied in the isoteniscope made it clear that such decomposition is appreciable even below 100°.

The values in the table below are given for every 5°, and were obtained graphically from the observed values.

TABLE I

Vapor Pressure of Tetranitro-methane.

Temperature Degrees	Pressure in mm Hg at 0°	Temperature. Degrees	Pressure in mm Hg at 0°
40	26.6	90	239
45	34.4	95	286
50	44.2	100	339
55	56.1	105	400
60	70.6	110	470
65	88.1	115	550
70	109	120	640
75	134	125	743
80	164	125.7	760
85	199		

Using the vapor-pressure curve thus defined to test the character of the liquid according to the criterion suggested by Hildebrand,[2] one obtains, using his units, a value of 13.9 for the entropy of vaporization divided by *R* at the temperature (near 70°) at which the concentration of the vapor is 0.00507 mole per liter. Assuming the vapor is normal, this would indicate slight, if any, association or abnormality in the liquid at this temperature.

PRINCETON, N. J.

[CONTRIBUTION FROM THE GEOPHYSICAL LABORATORY OF THE CARNEGIE INSTITUTION OF WASHINGTON.]

ELECTROMETRIC TITRATIONS, WITH SPECIAL REFERENCE TO THE DETERMINATION OF FERROUS AND FERRIC IRON.[3]

BY J. C. HOSTETTER AND H. S. ROBERTS.

Received July 12, 1919

Introductory.

In the study of the oxides of iron now in progress at the Geophysical Laboratory, it has become increasingly evident that the ordinary methods for determining small amounts of ferrous oxide in the presence of much ferric oxide are not susceptible of the precision attained in some of the other measurements on the oxides, as, for instance, that of magnetic susceptibility.[1] Especially was it necessary to be able to distinguish accurately between the ferrous iron contents of ferric oxides when the latter contained less than 0.1% FeO,[2] since easily measureable differences in the magnetic susceptibilities of such oxides have been found. The method which is described herein permits of the determination of a few tenths of a milligram of ferrous iron in the presence of any quantity—up to 100 g.—of ferric iron. The essential details of this method were developed before the entry of the United States into the war and, extended to include the determination of total iron, the method found many applications in the determination of iron in raw materials for optical glass, in optical glasses themselves, in glass pots, and, to quote an example in quite a different field, in the determination of iron in sulfur chloride.[3]

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[1] See THIS JOURNAL, 32, 1412 (1910).

[2] THIS JOURNAL, 37, 970 (1915).

[3] Read at the Buffalo Meeting of the American Chemical Society, April 9, 1919.

This method is, in brief, the direct electrometric titration of the ferrous iron with standard dichromate. The various factors affecting this determination have been studied in some detail and as sharp end-points can now be obtained with 0.01 *N* or even with 0.0005 *N* dichromate solutions as with the more concentrated solutions usually employed. Furthermore, the technic of the method for larger quantities of ferrous iron has now been developed to such an extent that oxidation and reduction titrations carried out electrometrically must hereafter be considered precision analytical methods capable of giving results to one part in a thousand or better.

Electrometric titrations for the determination of various elements have been proposed from time to time and some excellent work of direct and indirect application to analytical procedure has been recorded in the foreign literature,[4] but not until the work of Hildebrand,[5] describing simplified apparatus, appeared in this country did the method receive much recognition. Shortly after the appearance of Hildebrand's paper came the work of Forbes and Bartlett,[6] who described an anomalous increase of potential produced by certain reducing agents and took advantage of this effect for conveniently locating end-points electrometrically. In

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[1] R. B. Sosman and J. C. Hostetter, *Trans. Am Inst. Mining Eng.*, 58, 409–433, 434–444 (1917).

[2] In previous publications it has been shown that Fe_2O_3 and Fe_3O_4 probably form a continuous series of solid solutions (Sosman and Hostetter, THIS JOURNAL, 38, 807–833 (1916)), and that all ordinary ferric oxides, both artificial and natural, carry determinable amounts of ferrous oxide

[3] At Edgewood Arsenal.

[4] R. Behrend, *Z. phys Chem.*, 11, 466–491 (1893); R. Peters, *Ibid*, 26, 193 (1898); C. Fredenhagen, *Z. anorg Chem.*, 29, 396–458 (1892); W. Böttger, *Z. phys. Chem.*, 24, 253–301 (1897); F. Crotognio, *Z. anorg. Chem.*, 24, 225–262 (1900); Ostwald, Luther and Drucker, "Physico-Chemische Messungen," p 454.

[5] THIS JOURNAL, 35, 847–871 (1913).

[6] *Ibid.*, 35, 1527 (1913).

1916 Kelley and Conant applied the latter method to the determination of vanadium,[1] and chromium,[2] in steels, making the method applicable to routine testing, and later Kelley and others developed compact apparatus[3] and extended the method to the determination of manganese.[4] Bichowsky[5] has titrated zinc with ferrocyanide and in the course of his investigations[6] was able to produce curves (volume of ferrocyanide against electromotive force) showing all variations from the "normal" curve to that described by Forbes and Bartlett.

In Hildebrand's work the end-point of the titration was taken as the point of inflection in the curve showing the relation between the voltage developed and the volume of oxidizer (dichromate) added Forbes and Bartlett, on the other hand, and later Kelley and Conant, simply made use of the greatly increased deflection of the galvanometer as an indication of the end-point, taking advantage of the increased sensitivity given by the anomalous rise. The latter method has been applied by these authors to routine work and with remarkable success. Our problem, however, was quite different and it seemed preferable to use the graphical method, as being of more general applicability. The time consumed in plotting is merely a matter of a few minutes and the shape of the curve is frequently of great value in indicating the presence of impurities—such as organic matter in hydrofluoric acid—in the solution being titrated.

Apparatus and Method.

The first set-up used was essentially that described by Hildebrand and the effects of certain variables were studied with it. After preliminary studies had demonstrated the successful application to our problems, apparatus was designed which permitted the thorough study of variables under controlled conditions Later also a simplified potentiometer was devised by Roberts,[7] the use of which eliminates the millivoltmeter from the set-up and makes the entire outfit very compact. This potentiometer is essentially a slide-wire and its successful use assumes that the voltage of the cell (dry cell or storage) remains steady or only shifts gradually during a titration, readings are taken as numbers proportional to the voltage.

Titrating Head.—A few words may be inserted here to describe the "titrating head" used to cover the flask which contains the solution to be titrated, in order that the atmosphere above the solution may be controlled, and also to support the calomel half-cell and the platinum electrode. Carbon dioxide or nitrogen (freed from oxygen) is passed through the flask before and during a titration; the entrance tube for carbon dioxide extends about half way into the flask. The calomel half-cell is made as shown in Fig. 1; the tube making connection with the solution has an internal diameter of about 1 mm. and is turned upwards at the bottom in order to prevent the heavy potassium or sodium chloride solution from running into the flask with a corresponding amount of lighter solution traveling up into the small tube and hence escaping the reaction. This connecting tube is not sealed to the titrating head but passes loosely through a tube which supports it, thus permitting adjustment for different sized flasks The calomel cell is made up with strong sodium or potassium chloride solution, such high concentration being desirable in order to reduce the resistance of the titrating system with consequent increase in electrical sensitivity and to raise its boiling point so that bubbles of steam may not form in the capillary. A small extension tube is sealed to the tip of the buret.

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[1] This Journal, 38, 341 (1916).

[2] *J Ind. Eng. Chem.*, 8, 718 (1916).

[3] *Ibid*, 9, 780 (1917).

[4] *Ibid.*, 10, 19 (1918).

[5] *Ibid.*, 9, 668 (1917).

[6] *J Wash Acad Sci.*, 7, 141 (1917).

[7] This Journal, 41, 1359 (1919)

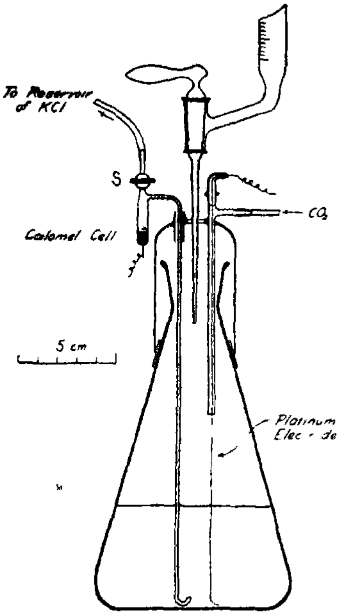

Fig 1 —Flask covered by "Titrating Head" which supports the calomel half-cell and platinum electrode and also permits the maintenance of a neutral atmosphere within the flask.

The electrode consists of a single platinum wire (0.4 mm. diam.) sealed into a tube ground into the carbon dioxide tube as shown in the sketch; this joint enables one to wash down the tube and electrode upon which solution may have spattered during the titration.

Method of Investigation.—The method of study followed here was, in its essentials, simply the electrometric titration of a few milligrams of ferrous iron under a variety of conditions, followed by comparison of the curves so obtained. The success of any titration in the preliminary experiments was judged by the character of the graph near the change of curvature and the precision with which the point of inflection could be determined. Later the quantitative side of the problem was studied. The results of the experiments defining conditions, recorded in this paper, are therefore expressed mainly in the form of curves.

Methods of Plotting.—The usual method of directly plotting the relations between volume of oxidizer V, and electromotive force E, is satisfactory for most cases. A convenient scale of coördinates which enables one to read the end-point with the precision ordinarily required as 1 cm. for 1 cc. against 1 cm. for 100 millivolts. In cases where the point of inflection is not readily determined on the graph plotted to this scale—as when too little acid is present during the titration—other ratios in which the voltage scale is increased may be used with advantage. A little practice enables one, however, to locate by inspection the point of inflection with the desired accuracy.

In some cases the plotting of $\Delta E/\Delta V$ against V is a distinct advantage; this derivative passes through a maximum at the point of inflection and consequently its relation to V may serve for the location of the end-point. Even such a curve as that of No. 4 in Hildebrand's paper,[1] which was caused by too low a concentration of acid in the solution being titrated and which he pronounced "unsatisfactory" can be made to yield a fairly satisfactory maximum corresponding to the point of inflection if $\Delta E/\Delta V$ instead of E is plotted against V. Reference to Fig. 2, which gives typical curves for the titration of ferrous iron by dichromate, shows the sharp maximum obtainable by plotting the derivative against volume.

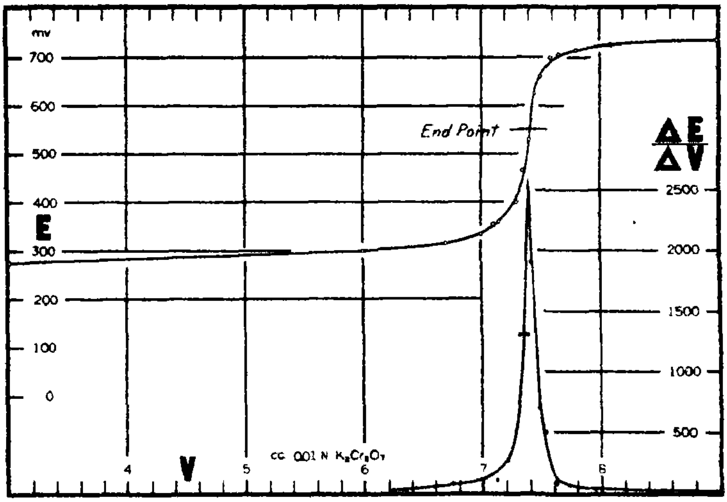

Fig. 2.—Titration of 4.1 mg. of ferrous iron in 70% conc. hydrochloric acid with dichromate solution yielding typical curve of potential E, against volume of dichromate, V. Plotting ΔE over ΔV gives a sharp maximum corresponding to the point of inflection which is the "end-point" of the titration.

The End-Point.

"Electrometric methods, unlike most of the other methods of volumetric analysis, are not merely special methods applicable to but one reaction under a rigorously limited set of experimental conditions as are our indicator methods, but they are perfectly general methods based not on the accident of the discovery of a new indicator but on a perfectly general principle. If we consider the reaction $A + B \longrightarrow C + D$ and introduce into the reaction mixture an electrode whose E. M. F. depends on the concentration of any of the reacting substances, say B the change of the E. M. F. as you add or subtract more or less of that substance is proportional not to the amount added but to the percentage change of concentration of that substance, and accordingly, the maximum percentage change of concentration and hence of E. M. F. occurs at the point where the concentration of B equals that of C, *i. e.*, occurs at the end-point (equilibrium point) of the reaction."[1]

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[1] *Loc. cit.*, Fig. 15, p. 870.

The shape of the curve relating electromotive force and concentration as the iron is oxidized follows from the logarithmic ratio of the concentrations in the well-known equation for the electromotive force of such cells. The voltage changes very slightly with the first additions of oxidizing agent, but as the one ion disappears the amount of oxidizing agent necessary to depress its concentration to, say 1% of its former value, rapidly becomes smaller. Just as soon as the concentration of one ion becomes negligibly small the reverse process takes place with respect to the oxidizing ion from the added reagent Up to this point the oxidizing agent has been reduced as rapidly as it was added and consequently no concentration of the oxidizing ion can develop until the reducing material is completely oxidized. When this point is reached the same reasoning will account for the increase of potential which is rapid at first as the concentration of the new ion increases slightly and then increases less rapidly as the concentration of the oxidizing ion increases. The point at which this change of direction occurs is obviously therefore the "end-point" of the particular reaction.

Experimental evidence that such a point of inflection actually corresponds to the end-point was obtained in two ways. In the first series definite amounts of ferrous iron were titrated electrometrically, and the quantities so determined, taking the point of inflection as the end-point, were checked against those known to be present. In the second series the titration of a ferrous solution with permanganate showed that the pink color indicating the end-point appeared exactly at the point of inflection when small quantities of ferrous iron were titrated in sulfuric acid solution. This subject will be referred to later.

Electrodes.—Experiments were made on electrodes of different materials and some of the curves obtained during this study are shown in Fig. 3. The "normal" curve is shown for purposes of comparison. These curves were obtained by carrying out a titration with several different wires immersed in the iron solution making readings on the different electrodes *seriatim*. Palladium is not suitable as an electrode for these titrations as evidenced by the curve of its electromotive force against dichromate; the voltage rises slightly at first and then remains constant, or nearly so, throughout the course of the titration.[1] The influence of palladium is also seen in the curve for the palladium-gold alloy which is intermediate between the palladium curve and that for gold, the latter electrode giving a comparatively small rise near the end-point. The curve shown here for platinum "B" which had been originally covered with platinum black was obtained only after repeated treatment of the electrode with acid. The improvement in the shape of the curve, which was initially, in other titrations, not much above that for palladium, was probably due to reduction of surface by solution[2] of the finely divided platinum black. In experiments with platinum electrodes of different area it was found that the best results, as evidenced by steadiness of potential and extent of rise near the end-points, were obtained with an electrode presenting the least possible surface to the solution. A small platinum wire (0.4 mm. diameter, for instance), was found to be satisfactory; it is used in the bright condition and between titrations is kept in 1 : 1 hydrochloric acid.

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[1] Quoted from an unpublished address by Dr. F. R. Bichowsky of this laboratory, before the Chemical Society of Washington, April 12, 1917.

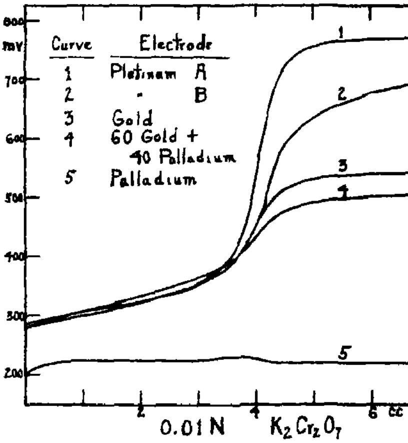

Fig 3.—Titration curves obtained with electrodes of different metals. The most satisfactory curve is given by platinum of small area (Curve 1).

Electrodes were found to be very sensitive to contamination—as a result of which very irregular curves are obtained, which are quite unsuitable solution was found to be about the same as that given with excess dichromate, under our conditions of acidity.

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[1] It is not unlikely that the curve for a palladium electrode will depend to some degree upon the amount of hydrogen, or other reducing gases, condensed within it. This, in turn would depend upon whether the electrode had been previously ignited in a gas flame, or by heating in air (as electrically). If curves of the type shown in No. 5 of Fig. 3 can be consistently reproduced (and there is much evidence that they can) the possibility is at once suggested that an electrode of palladium can be substituted for the calomel electrode with a considerable simplification of apparatus.

[2] It is interesting to note in this connection that a bright platinum foil electrode presenting approximately 5 sq. cm. area to the solution, lost 0.17 mg. during a titration carried out in strong HCl In this case, however, the solution was exposed to the air.

Hydrofluoric Acid.—Two series of titrations of ferrous iron in the presence of hydrofluoric acid accompanied by hydrochloric acid and also by sulfuric acid showed that hydrofluoric acid was without detrimental effect. Its inertness indicated that the method could be applied to the direct determination of ferrous oxide in silicates and subsequently many glasses and glass pots were analyzed for ferrous iron in this manner. In the course of his work on the analysis of optical glasses, our colleague, J. B. Ferguson, obtained some irregular results when hydrofluoric acid was present in the iron solution during titration and later this was traced to the presence of impurities (probably organic matter), in the hydrofluoric acid; the organic matter was oxidized slowly by dichromate and gave a sloping curve which somewhat obscured the point of inflection. Some lots of acid showed this irregular action while others gave smooth, normal curves. This subject will be considered more in detail elsewhere.

Effect of Acidity when Using Dilute Dichromate.—From the data just presented it is evident that the electrometric titration of ferrous iron may be successfully carried out in solutions of widely varying acidity for concentrations of dichromate in the range of 0.1 *N* to 0.005 *N*.

When using 0 001 *N* dichromate, however, the acidity and volume of the iron solution become highly important. The curves obtained on titrating with *0.001 N dichromate, iron solutions containing 0.56 mg. ferrous iron* in 10 and also in 35 cc. of 25% sulfuric acid, showed very little rise of potential and, at best, gave an obscure end-point. On the other hand, good curves may be obtained with 0 001 *N* and even 0.0005 *N* dichromate if this has been made up with acid, and if the volume of solution to be titrated is small. The solid curves of Fig. 6 represent the titration of about 0.56 mg. metallic iron in various amounts of 25% conc. sulfuric acid; the oxidizer in each case was 0.001 *N* dichromate in 25% conc. sulfuric acid, about 10 cc. being required to reach the end-point. This series illustrates the advantage of working with a small volume. The dotted curve is taken from the titration of half this quantity of iron in 10 cc. of 25% conc. sulfuric acid, the oxidizer in this case being 0.0005 *N* dichromate in 25% sulfuric acid.

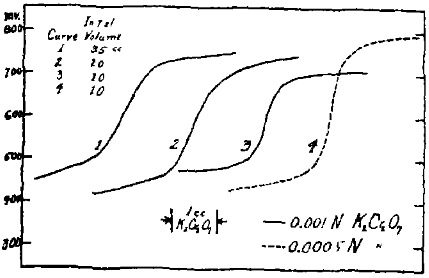

Fig. 6.—Titrations with 0 001 *N* and 0 0005 *N* potassium dichromate.

Effect of Ferric Iron on the Titration of Ferrous Iron.

After the preliminary work on the effects of acidity had been completed, titrations of small amounts of ferrous iron were carried out with the addition of successively larger portions of ferric iron. The result, as was to be expected, was a shortening of the difference in potential at the end-point, mainly because of the increased initial potential. The potential at the point of inflection was also increased under these conditions. However, the points of inflection were still perfectly sharp even at the higher concentrations of ferric iron as is evident from the curves given in Fig. 7. The ferrous iron titrated in the last curve was only 1 part to 2600 ferric. In the work on the determination of ferrous iron in ferric salts the ferrous iron content titrated directly was at times only 0.0002% (of the salt) and even under these extreme conditions the end-point obtained was perfectly definite.

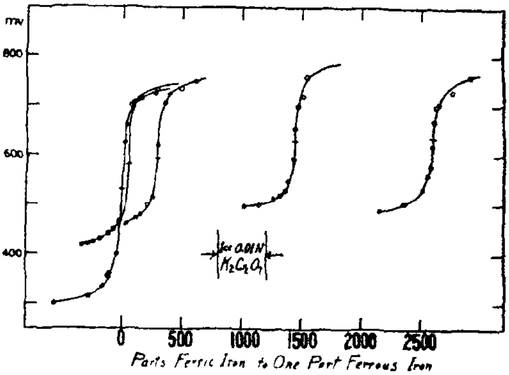

Fig. 7.—Change in titration curve of ferrous iron caused by additions of ferric iron. The change of potential near the end-point is reduced as the ratio of ferric iron to ferrous increases but the end-point is still easily located

Determination of Ferrous Iron In Ferric Compounds.

Conditions having been established for the determination of ferrous iron in the presence of large quantities of ferric iron the former was determined in a number of ferric salts. In order to dissolve the ferric compound in the absence of air the solution was effected in an atmosphere of carbon dioxide in the dissolving flask shown in Fig. 8. This is a modification of the one formerly used[1] and possesses the additional advantage that spatterings on the combination stopper and funnel can be more readily washed off.

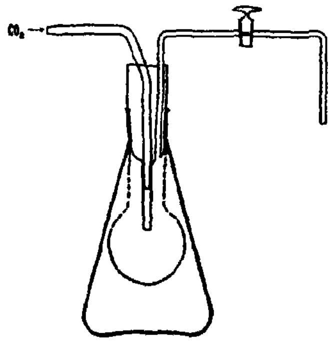

Fig. 8.—Flask for dissolving salts or oxides in an inert atmosphere.

Method.—Ten g. of the salt (sulfate or chloride) is dissolved in water in an atmosphere of carbon dioxide and the solution treated with an equal volume of conc. hydrochloric acid. The funnel-stopper of the flask is now removed and the titrating head put in place, the stream of carbon dioxide through the flask continuing to flow. Electrical connection is made by allowing the capillary connecting with the calomel cell to fill by manipulating the small stopcock shown at S in Fig. 1. The solution is now titrated with 0.01 *N* potassium dichromate and the results plotted.

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[1] R. B. Sosman and J. C. Hostetter, This Journal, 38, 822 (1916).

TABLE I.—FERROUS IRON IN FERRIC SALTS.
By Electrometric Titration

Ferric salt.	Maker	Grade	Lot No	% ferrous iron.
Ammonium sulfate.	J. T. Baker	C. P. analyzed	102711	0.0005
Ammonium sulfate .	Baker & Adamson	C. P. analyzed	.	0.0035
Ammonium sulfate.	Baker & Adamson	C. P. analyzed		<0.0005
Ammonium sulfate..	Baker & Adamson	C. P analyzed		<0.0005
Ammonium sulfate .	Baker & Adamson	C. P analyzed	.	0.010
Ammonium sulfate.	Kahlbaum	White label	P 2112	0.00025
Ammonium sulfate...	Squibb	Reagent	12098	<0.0002
Bromide..........	Kahlbaum	White label	Z 3012	5.41
Chloride:				
Hydrated crystals..	J. T. Baker	C P analyzed	12611	0.0005
Hydrated crystals .	J T. Baker	C P. analyzed	32913	0.0005
Hydrated crystals.	Baker & Adamson	C P. analyzed		0.0022
Hydrated crystals.	Baker & Adamson	C P. analyzed	..	0.004
Hydrated crystals.	Eimer & Amend	Pure		0.004
Hydrated crystals	Kahlbaum	"Zur analyse"	. [1]	0.0014
Hydrated crystals.	Kahlbaum	White label	D 0708	0.0005
Hydrated crystals .	Squibb	Reagent	17453	0.004
Sublimed...... .	Baker & Adamson	C P. analyzed	.	[2]
Sublimed........	Kahlbaum	White label	C 070?	0.404
Sublimed	Merck	Reagent	S 3597 12716	0.020
Sulfate	J. T. Baker	C. P analyzed	12315	<0.0003

The change of voltage with the first drop of dichromate is, in itself, an excellent criterion as to the presence of ferrous iron. The curves of Fig. 9 show the change in the form of the curve in the titration of successively increasing small amounts of ferrous oxide. Ferric iron was present to the extent of 1660 mg. in each titration. The scale of volumes in Fig. 9 is much larger than in the other figures.

Results on the percentage of ferrous iron in a number of ferric salts have been collected in Table I, which shows a considerable variation in ferrous iron content. The salts analyzed were taken from our stock shelves; the ferrous iron varies from 0.0003 to 0.020%, although there are several exceptions.

It should be pointed out here that the percentages of ferrous iron reported in these ferric salts were of necessity determined in solution and some proportion of the ferrous iron found may have arisen from action of the solvent on a solid salt—in which the iron was all in the "ferric" condition—by attainment of equilibrium between ferrous and ferric iron. This would arise as a consequence of the relation developed by Peters:[1] these two ions are in equilibrium and the concentration of one does not normally reach zero. Ferrous iron might form by hydrolysis also, since the hydrolysis of ferric salts, especially the chloride, probably involves the formation of intermediate ions containing ferrous iron.[2] The amounts of ferrous ion developed by these reactions are small under our conditions, but it should be constant, under identical conditions, for each type of salt. Since, however, variations in ferrous iron content of these salts were actually found, differences must have existed in the salts themselves. The lowest values found may have been formed as indicated above, but it is unlikely that the larger percentages can be accounted for in this manner.

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[1] Not distinguishable.

[2] Contains metallic iron

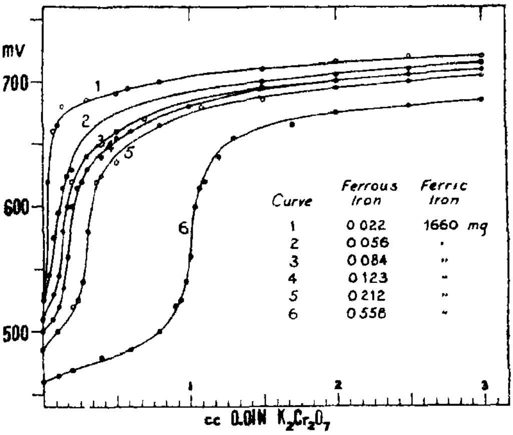

Fig 9—Small amounts of ferrous iron titrated in the presence of 1660 mg. ferric iron.

A number of old samples of ferric chloride which had stood loosely stoppered on the stock room shelves for possibly 10 years were examined and some observations on these may be of interest. The salt in one of these bottles was covered with a layer of saturated solution; 10 g. of the moist salt was found to contain 0 11 mg. of ferrous oxide, whereas 3 cc. of the solution over the salt gave 0.16 mg. Expressed on the basis of total iron the salt contained approximately one part ferrous iron in 30,000 while the solution in contact with it showed double this amount. Hydrolysis involving the formation of an intermediate ferrous ion would account for the higher percentage in the solution.

Reduction of Ferric Chloride by Boiling.—The following experiment is interesting in showing that the small amount of ferrous iron formed by reduction on boiling aqueous ferric chloride in ordinary air may be readily determined electrometrically. While no special precautions were taken to insure the absence of traces of reducing material from the water or the air, the results indicate that the solution was reduced notwithstanding the ease with which the air oxidizes ferrous solutions containing chloride. A solution of ferric chloride (10 g. crystals in 50 cc. water) was boiled in a flask for 5 minutes, after which the solution was allowed to stand on the hot plate for 30 minutes. Some precipitation of ferric hydrate took place during this treatment. This precipitate was dissolved when the solution was treated with 100 cc. of conc. hydrochloric acid previous to the titration. The solution now showed 0.76 mg. ferrous iron. Ten g. of the salt dissolved and titrated without having been boiled showed 0.22 mg., the difference of 0 54 mg. having developed during the treatment at the higher temperature, notwithstanding the fact that the solution was freely exposed to the air during this time. Other similar experiments confirmed this.

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[1] *Loc. cit.*

[2] H. M. Goodwin, *Z. phys. Chem.*, 21, 1–15 (1896); W. Spring, *Rec. trav. chim.*, 16, 237–249 (1897).

The similar reaction in the case of ferric bromide has been known for many years.[1]

Ferric Oxides.—Several determinations of ferrous oxide in ferric oxides from different sources are given in Table II; the ferrous iron was determined in a solution of 10 g. of the oxide dissolved in 1 : 1 hydrochloric acid. The last 3 oxides were produced by ignition of certain salts over the blast lamp. This ignition was carried out in platinum using an asbestos board screen to carry away reducing gases. The small amounts of ferrous oxide (0.024 to 0.055%) found in the ignited product are formed by reduction in one or all of the following ways: namely, (1) reduction by platinum,[2] (2) by reducing gases from the flame, (3) by dissociation of ferric oxide even in air.[3] The magnetic susceptibilities of these oxides were previously determined and confirm the presence of ferrous oxide.[4]

The Determination of Large Amounts of Ferrous Iron.—The method previously discussed may be applied equally well to the determination of large quantities of ferrous iron if the accuracy given by volume buret is sufficient. For higher precision,

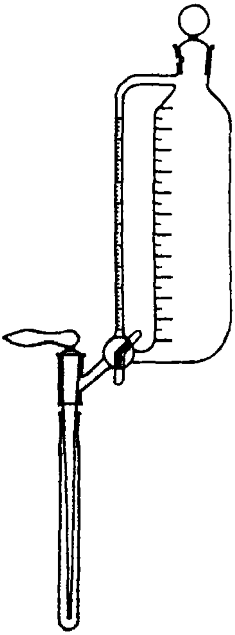

Fig. 10.—Modified weight buret for electrometric titrations. The small volume buret sealed to the weight buret is used for titrating near the end-points.

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[1] L. L. DeKoninck, *Z. angew. Chem.*, 3, 149 (1889).

[2] Robert B. Sosman and J. C. Hostetter, *J. Wash. Acad. Sci.*, 5, 293–303 (1915).

[3] J. C. Hostetter and R. B. Sosman, THIS JOURNAL, 38, 1188–1198 (1916).

[4] R. B. Sosman and J. C. Hostetter, *Trans. Am. Inst. Mining Eng.*, 58, 418 (1917).

the only necessary modification in the method is the use of a weighing buret[1] for the dichromate solution.

The inconvenience of weighing the buret and solution after the addition of each drop near the end-point may be avoided in two ways. The first method uses strong oxidizing solution (as 0.1 *N*) for the entire titration; the solution is delivered, however, from the modified weighing buret shown in Fig. 10. This buret permits the use of a small volume buret (1 cc. capacity reading to 0.01 cc.) for the end-point while the larger reservoir is drawn upon for most of the titration. The manipulation of the buret is obvious from the figure. The weight of solution corresponding to the unit graduation must, of course, be previously determined.

TABLE II.—FERROUS OXIDE IN FERRIC OXIDES FROM DIFFERENT SOURCES.

Source of ferric oxide	% FeO
Merck, Iron Oxide Reagent (Lot 1041) (from Nitrate)	0.015
Kahlbaum, Eisenoxyd "Zur Analyse mit Garantieschein" (Lot 4478)	0.033[2]
Ignition over blast lamp of	
Ferric Nitrate (J. T. Baker)	0.055
Ferric Hydrate, C. P., Moist (J. T. Baker)	0.024
Ferrous Sulfate (J. T. Baker)	0.050

The second method for titrating with strong dichromate is the use of the weighing buret until the voltage indicates the proximity of the region of inflection, after which the titration is completed with a dilute solution

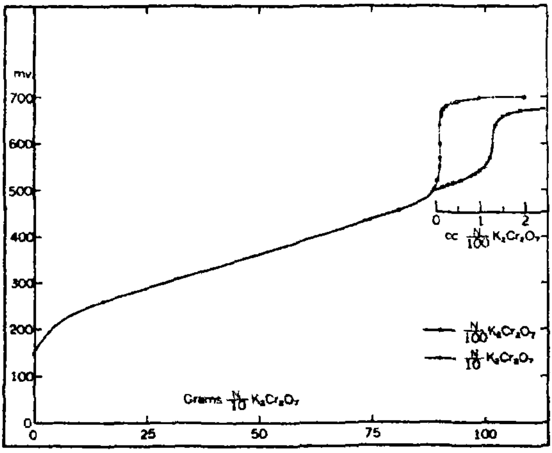

Fig. 11.—Method of plotting results when 0.01 *N* dichromate solution, delivered from a volume buret, is used for the end-point region, while 0.1 *N* dichromate solution, from a weight buret, is used for most of the curve.

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[1] This buret should have an extended tip sealed to it and the protecting cap should be lengthened correspondingly.

[2] Not homogeneous; some portions contain as much as 0.043% FeO.

delivered from a volume buret. For convenience and also in order to minimize errors in the graduations of the buret, the dilute solution is made up so that 1 cc. corresponds to 0.1 g. of the stronger solution. The plot of the dilute solution against voltage is made on a scale such that the point of inflection can be located to within 0.02 to 0.04 cc., corresponding to 0.002 to 0.004 g. of the more concentrated solution (see Fig. 11). It is thus seen that the end-point error is reduced to a minimum by this procedure, giving the possibility of a precision in titrations of this kind greater than that attained by the use of other methods.

TABLE III.—ELECTROMETRIC TITRATION OF LARGE AMOUNTS OF FERROUS IRON.
Metallic Iron (Electrolytic, Langbein-Pfanhauser)

Weight. G.	Acid.	Weight 0.1 *N* $K_2Cr_2O_7$. G.	"Iron value." Fe per g. $K_2Cr_2O_7$ soln. G.
0.5107	HCl	91.555	0.005578$_0$
0.5163	HCl	92.560	0.005578$_0$
0.4693	HCl	84.201	0.005573$_6$
0.4479	HCl	80.267	0.005580$_1$
0.3858	H_2SO_4	69.165	0.005577$_9$
0.5235	H_2SO_4	93.875	0.005576$_1$
0.5449	H_2SO_4	97.750	0.005574$_4$
		Av.,	0.005576$_9$

The results given in Table III were obtained by the second method described above. Electrolytic iron (rolled sheet from Langbein-Pfanhauser) was dissolved in acid in an atmosphere of carbon dioxide and hydrogen without any other special precautions and the solution so obtained titrated directly. The figures shown in the table as "iron-value" of the dichromate merely indicate the ratio of dichromate to this iron for comparative purposes. The maximum error in this series is 1 part in 800. The deviations in this series could have been reduced by first reducing electrometrically, with stannous chloride as described below, the small amount of ferric iron formed in the solution, probably from dissolved oxygen in the acid and water used to effect solution of the iron. Inasmuch as our primary interest was the determination of small amounts of iron the work on large quantities was not continued further.

Electrometric Titration of Ferric Iron with Stannous Chloride.

The direct determination of ferric iron by titration with stannous chloride has previously been carried out by utilizing the disappearance of the yellow color[1] or the action on methylene blue[2] as the end-point. Electrometrically this titration may be carried out very successfully. Fig. 12 shows a curve relating voltage and volume of stannous chloride (0.005 *N*) used in a typical titration of ferric iron. The voltage change at the end-

[1] W. W. Scott, "Standard Methods of Chemical Analysis," 1917, p. 221.

[2] C. Russo, *Gazz. chim. ital.*, 44, 1–8 (1914)

point is from about +250 millivolts to —100. This change in sign necessitates a reversing switch in the circuit or, more conveniently, the location of the "zero" point on the potentiometer at some distance from one end as has been done in the instrument described by Roberts.

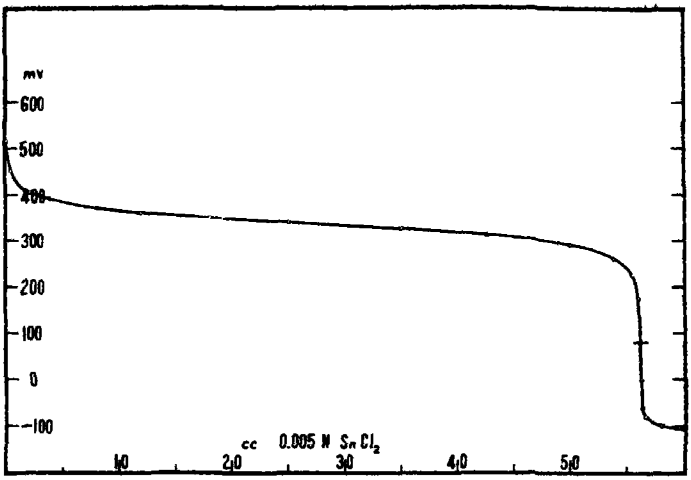

Fig 12.—Electrometric titration of ferric iron with 0.005 N stannous chloride solution.

Determination of Ferric Iron in Ferrous Salts.—The titration just described enables us to determine directly small amounts of ferric iron in the presence of ferrous iron, and, as an application of this method, determinations were carried out on ferrous salts. These salts are frequently used as convenient standards in oxidimetry and a knowledge of the ferric iron content is necessary if a correct standardization is to be made. Table IV summarizes a few results showing the percentages of ferric iron in freshly opened ferrous salts and also in bottles which have stood loosely stoppered for some years. The error introduced, when using such a salt as a standard, by assuming that all of the iron is ferrous, is indicated in the last column of the table, in which the ferric iron is calculated to the percentage of total iron.

TABLE IV.—FERRIC IRON IN FERROUS SALTS OF REAGENT QUALITY

Salt	Bottle [1]	Maker	Lot No.	% ferric iron in salt.	 of total iron.
Ferrous ammonium sulfate.	Sealed	J. T. Baker	61013	0.028	0.20
Ferrous ammonium sulfate.	Opened	J. T. Baker	61013	0.047	0.33
Ferrous ammonium sulfate.	Opened	J. T. Baker	6211	0.043	0.30
Ferrous sulfate....	Sealed	Squibb	7624	0 08	0 41
Ferrous sulfate............	Opened	Baker & Adamson	...	0 22	1 10

[1] *Sealed* (by maker); *Opened* (loosely stoppered for at least 2 years).

The stannous chloride solution is conveniently standardized by electrometric titration against dichromate as described below.

Electrometric Titration of Potassium Dichromate with Stannous Chloride.

The electrometric titration of dichromate with stannous chloride, or the reverse titration, may be readily carried out with the same apparatus. The titration is made in acid solution at an elevated temperature since the reaction proceeds rather slowly at room temperature. Inasmuch as the reaction is between a very strong oxidizer and a powerful reducing agent, the voltage change is very large, namely, from about +600 mv. to —100 mv. Fig. 13 shows a typical curve for this titration.

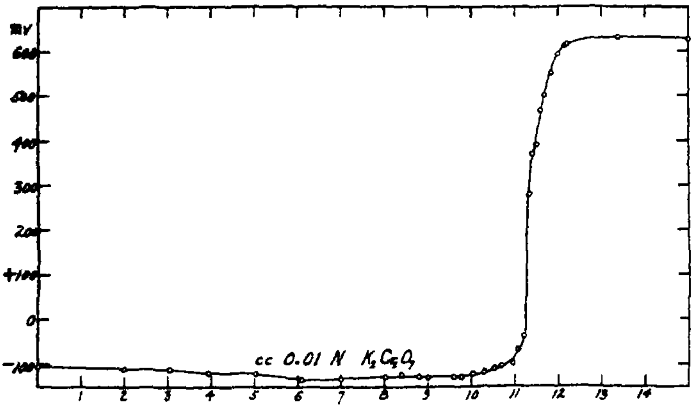

Fig. 13.—Electrometric titration of stannous chloride with potassium dichromate solution.

Combination Method for the Determination of Total Iron.

The two reactions just described may be readily combined in one operation to give total iron. In this determination the iron solution is completely reduced, as shown by the color change as well as by voltage, with concentrated stannous chloride solution which is added in slight excess. The solution (at 70° or 80°) is now oxidized with standardized dichromate solution plotting E. M. F. against volume as usual. The resulting curve shows two points of inflection. The first point indicates when the excess of stannous chloride is used up and the second corresponds to the complete oxidation of ferrous iron. The volume of dichromate between these two end-points obviously represents that required by the iron.

The shape of the curve and the effect of varying concentrations of hydrochloric acid are shown in Fig. 14.

Applications of Method for Total Iron.

The method just described has been successfully used in the determination of iron in raw materials for optical glass—such as sand,[1] sodium and potassium salts, barium carbonate, zinc oxide, borax and boric acid, and the oxides of lead. None of these substances interferes with the method, although when iron is determined in a nitrate it must be precipitated first as hydroxide[1] in order to separate it from the interfering nitric acid.

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[1] John B. Ferguson, *J. Ind. Eng. Chem.*, 9, 941 (1917).

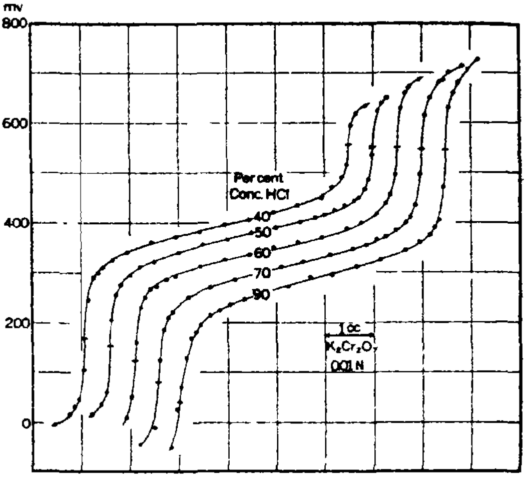

Fig. 14.—Electrometric titration of iron which has been reduced with slight excess of stannous chloride. The amount of dichromate solution corresponding to the iron is the volume between the two end-points

It is obvious that such metallic oxides as are not reduced by stannous chloride need not interfere with this method of determining total iron. Actual tests made in the presence of manganous manganese and titanium (as TiO_2) show definitely that these exert no deleterious effect on the titration; vanadic oxide, on the other hand, is reduced by stannous chloride and consequently must be determined separately and deducted from the total of iron and vandium.

Application of Electrometric Method to the Determination of "Blanks."

In their paper Bartlett and Forbes[2] show the magnitude of the errors inherent in the use of an outside indicator when titrating with dichromate. They were enabled to do this by simultaneously studying the titration electrometrically and also with the outside indicator. In similar manner much information may be gained by electrometrically studying such reactions as permanganate titrations. Fig. 15 shows curves obtained when titrating ferrous iron with permanganate under different conditions of acidity, and different concentrations of ferric iron, which are somewhat representative of conditions frequently met in actual practice. Curve 1, where 2.87 mg. of ferrous iron was titrated with 0.01 N potassium permanganate in 17% conc. sulfuric acid shows the development of the pink end-point at the exact point of inflection. The presence of 28.7 mg. of ferric iron (as sulfate) in a similar solution containing 8% conc. sulfuric acid masked the pink color of the end-point to such an extent that the color change did not take place until after the point of inflection was passed by 0.35 cc.; which, therefore, represents the "blank" for these conditions (Curve 2). The titration of the same amount of ferrous iron in the presence of 57.3 mg. ferric iron in phosphoric acid (2.5% by volume of the 85% acid) was free from blank (Curve 3) even though the amount of ferric iron was double that present in the previous titration represented in Curve 2. Adding 5% conc. sulfuric acid to the phosphoric acid solution gave a blank of 0.07 cc. potassium permanganate (Curve 4) with other conditions, such as ferric iron content, identical. Curve 5 represents the titration of 2.87 mg. ferrous iron in the presence of 250 mg. ferric iron, added as chloride, and 6% of titrating mixture.[1] The blank was greatly increased here—amounting to about 0.50 cc., which was changed but slightly by the addition of 0.5% conc. hydrochloric acid. Other data on these titrations are presented in Table V.

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[1] A small amount (1 cc.) of saturated alum solution is added before precipitation in order to ensure complete separation of the ferric hydroxide.

[2] This Journal, 35, 1527 (1913).

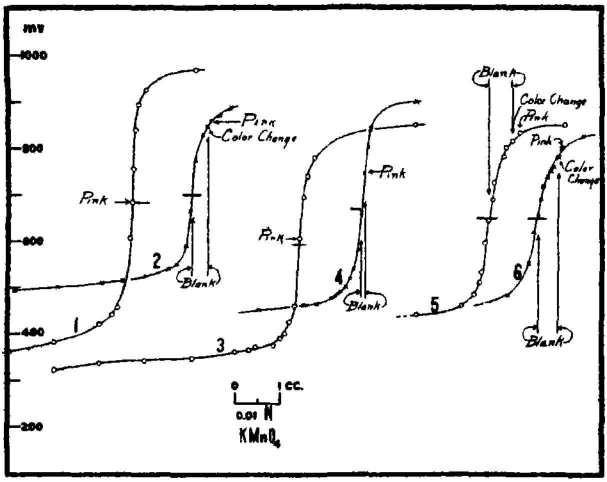

Fig. 15.—Electrometric titrations of ferrous iron with 0.01 N permanganate solution. The volume of permanganate solution required to give a color end-point after the point of inflection has been passed represents the "blank" for those particular conditions.

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[1] Bur. Standards, *Circ.* 26 (2nd Ed.), 11 (1911).

TABLE V.—ELECTROMETRIC TITRATIONS WITH 0.01 *N* PERMANGANATE.
(Ferrous Iron = 2.87 Mg.)

Curve No (Fig. 14.)	Total volume. Cc.	Ferric iron added. Mg	Acidity conditions	"Blank" 0 1 *N* $KMnO_4$. Cc.
1	150	0.0	17% sulfuric (conc.)	0.0
2	200	28.7	10% sulfuric (conc.)	0.35
3	200	57.3	2.5% phosphoric (85%)	0 0
4	200	57 3	2.5% phosphoric (85%) and 5.0% sulfuric (conc.)	0 07
5	215	250	6% titrating mixture. Ferric iron added as chloride	0 50
6	220	250	6% titrating mixture. 0 5% hydrochloric (conc.). Ferric iron added as chloride.	0.45

Summary.

The advantages of the electrometric method for oxidizing and reducing reactions may be summarized as follows:

1. This method permits the use of potassium dichromate with its numerous advantages.

2. The reduction of the solution with electrometric control eliminates the removal of excess reducing agent which must be done with the usual methods of reduction.

3. Conditions, such as acidity, need not be controlled except within very wide limits, and hydrochloric, sulfuric or hydrofluoric acid, or mixtures of these, may all be used. In contrast to these wide limits, note the narrow acid limits (1.5 to 2 5% by volume of sulfuric acid) within which the reduction with sulfur dioxide or hydrogen sulfide must be carried out[1] and the precautions which must be taken in a permanganate titration in the presence of either chlorides or fluorides.

4. The sensitivity and accuracy of the method make possible (*a*) the determination of a few tenths of a milligram of tin, chromium, ferrous or ferric iron, and probably many other elements, in the presence of large quantities of some other element, and (*b*) the determination of blanks involved in some of the ordinary determinations by reducing or oxidizing agents.

5. The time within which a determination can be carried out is greatly shortened. The content of ferrous and ferric iron in a silicate, for instance, can be determined in from 15 to 30 minutes.

6. The precision attainable is comparable to the best of the ordinary volumetric determinations.

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[1] W. F. Hillebrand, "Analysis of Silicate and Carbonate Rocks," U. S. Geol. Surv., *Bull.* 422. See page 107 for reference to H_2S; work of R. S. McBride on SO_2 quoted in footnote on page 108.

[CONTRIBUTION FROM THE GEOPHYSICAL LABORATORY OF THE CARNEGIE INSTITUTION OF WASHINGTON.]

ELECTRICAL APPARATUS FOR USE IN ELECTROMETRIC TITRATION.

BY HOWARD S. ROBERTS

Received July 14, 1919

The increasing use of the electrometric method of locating end-points in certain titrations has made it seem pertinent to discuss and describe suitable electrical apparatus for the purpose. The choice of apparatus is rendered very different from that of potentiometric apparatus for other purposes because of the following facts: (1) We are interested here in relative rather than absolute values of the electromotive force developed during the titration; (2) the electromotive force frequently changes sign;[1] and (3) the apparatus must often be used in an atmosphere charged with acid fumes.

The end-point of the titration is located at a point of inflection of the curve obtained by plotting, against the volume of titrating solution added, the electromotive force developed between an electrode immersed in the solution being titrated, and another, whose potential remains constant.[2] The latter is generally a calomel half-cell, connected through a capillary to the solution being titrated.

The potentiometer used by Hildebrand[3] consisted of a millivoltmeter shunting a variable resistance. Except for the fact that the electromotive force of the potentiometer battery is uncertain and variable, the variable rheostat might well be calibrated directly in millivolts, and the millivoltmeter omitted. It will be shown later that the variation of the battery is unimportant and that the rheostat may be calibrated in any unit whatever, provided the indications of its scale are practically proportional to the potential drop across it.

The change of voltage at the end-point is so great, under appropriate conditions, that the potentiometer may merely be balanced at the beginning of the titration, and the end-point located by the large, permanent galvanometer deflection that accompanies this change.[4] Apparatus for use with this method as applied to the determination of chromium, manganese and vanadium has been designed by G. L. Kelley and others[5] and has been put on the market.[6]

For more precise work, the end-point of the titration can always be located much more closely by plotting. Moreover, many substances likely to be present in the solution cause the change of the electromotive force at the end-point to be so slow that plotting is absolutely essential.[1] Thus the usefulness of the Kelley apparatus would be greatly extended by the presence of a scale of equal parts on the potentiometer proper.

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[1] When titrating with $SnCl_2$, for example.

[2] J Hildebrand, THIS JOURNAL, 35, 847–871 (1913).

[3] *Loc cit*, p. 851

[4] G S Forbes and E P Bartlett, THIS JOURNAL, 35, 1527 (1913), G. L. Kelley, *J. Ind. Eng Chem*, 9, 780 (1917).

[5] *J. Ind Eng Chem*, 9, 780 (1917)

[6] Leeds and Northrup Co., *Bull.* 498.

If we plot electromotive forces as ordinates against amounts of titrating solution as abscissas it is obvious that the whole curve may be shifted up or down without changing the abscissa of the point of inflection. Moreover, since the coördinates of the point of inflection are independent of the scale chosen in plotting the curve, the electromotive force may be measured in any unit whatever, whose actual value need not even be known.

From these conditions we see that our potentiometer may be provided with a scale, of an arbitrarily chosen unit, whose zero is so placed that the scale readings are always positive although the electromotive force developed by the potentiometer changes from negative to positive as the

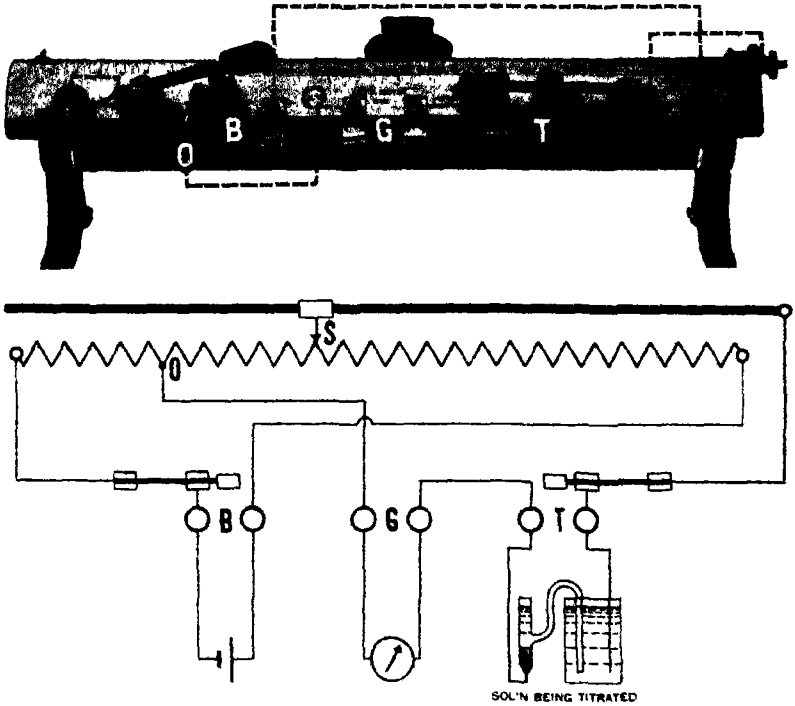

Fig. 1.—Photograph and diagram of simplified potentiometer for use in electrometric titration.

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[1] Hostetter and Roberts, This Journal, 41, 1337 (1919).

slider is moved along the scale. This condition can be attained by taking off a tap at a suitable point along the potentiometer winding, as at O in Fig. 1. This method has the very distinct advantage of making it unnecessary to use a reversing switch when the electromotive force being measured changes sign. It also does away with the necessity of writing (or forgetting) the minus sign before some of the readings.

Experience has shown that the electromotive force developed by the potentiometer may vary 5% from being proportional to the scale reading, provided the variation does not change abruptly by an amount greater than 1%. The voltage of the potentiometer battery may be permitted to change even more than this during the course of a titration without causing trouble, because this change, being the result of polarization, is gradual and will therefore have very little effect on the shape of the curve. Thus an ordinary dry cell may be used, though the resistance of the potentiometer should in this case be 50 ohms or more in order that the dry cell may have a long life. A single storage cell gives a much more constant electromotive force, but is not essential.

The potentiometer shown in Fig. 1 was made by fitting a boxwood ruler to a well known type of rheostat,[1] and mounting the battery switch, galvanometer switch and terminals on the ruler. Its resistance is 325 ohms. The tap at the point O is made with a fine, stranded wire soldered to one turn of the rheostat winding and reinforced with a drop of De Khotinsky cement over the solder All of the connections are on the under side of the ruler and are indicated by dotted lines in the photograph. This particular rheostat, when used with a single dry cell, will measure electromotive forces between about—0.3 volt at a scale reading of 25 mm. and +1.0 volts at a scale reading of 275 mm.

While several of these potentiometers have been in use for over two years and have proven entirely satisfactory, it has seemed desirable to find an alternative style of rheostat for them. This has been found, in the form of a "tuning coil" for amateur wireless work. It is shown diagrammatically in Fig 2, and its connections are indicated. This rheostat has two sliders, each of which may be provided with a scale. The scale readings may all be made positive by numbering the two scales in opposite directions, and arranging them so that when the two sliders are set on the last turn of wire to the left the reading on both the scales will be alike. Stops of some sort may be provided to stop the sliders at this turn. One or the other slider is always left at this point, and a balance obtained by shifting the second, one slider being used for positive electromotive forces and the other for negative. If the near slider, S′ in Fig. 2, is placed at the extreme left as shown in the figure and the far slider S then moved from the position in Fig. 2 to the extreme left, the potential difference between the two sliders will increase from its original negative value to zero, while the scale reading will increase to 100, and the readings on both scales now will be 100. If the far slider S is now left at 100, and the near one S′ moved to the right, the potential difference will increase from zero to some positive value, while the scale reading will increase from 100 to some higher value.

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[1] "Jagabi," purchased from J. G Biddle, Philadelphia.

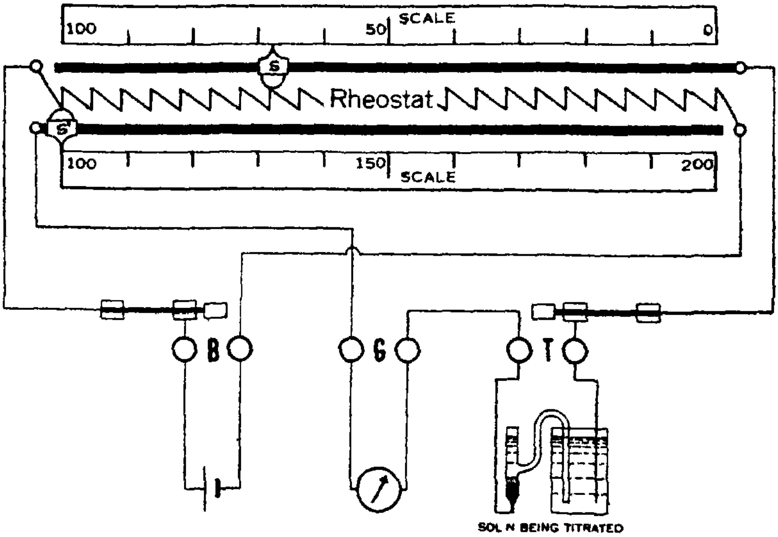

Fig 2.—Diagram of common wireless tuning coil used as a potentiometer for electrometric titration

The disadvantage of this rheostat lies in the fact that it is wound with copper wire. The coil not only corrodes readily, but the resistance, a very few ohms, is so low that the dry cell used with it does not last very long. However, it may readily be rewound with resistance wire which will correct both of these defects. Some such wire as chromel, nichrome, etc., is best for this purpose because the coating of oxide on the wire provides ample insulation between the turns. An approximate calibration curve can readily be constructed for either of these potentiometers. The voltage in millivolts of the battery, divided by the length in scale divisions of the rheostat winding, gives the value of one scale division in millivolts. The voltage represented by any point on the scale is then the product of this value by the distance to the zero point of the scale, *i. e.*, the point at which the slider and tap-off, or the two sliders, as the case may be, make contact with the same turn of wire.

A millivoltmeter may be connected to the slider and tap-off, or to the two sliders, as in Hildebrand's potentiometer; but it must be borne in mind that a calibration of the potentiometer can not be made in this way because of the shunting effect of the millivoltmeter.

The Galvanometer.

As the resistance through the solution and capillary is often several thousand ohms, the galvanometer should have a rather high resistance—so high as to make it impracticable to substitute an ordinary millivoltmeter. It need not be very sensitive; 1 to 2 megohms is sufficient. A much greater sensitivity than this is to be avoided because of the tendency for the pointer to be deflected off the scale and to follow the insignificant changes of electromotive force due to stirring, etc. It should have a short period to facilitate rapid work. The other considerations are dictated by resistance to acid fumes, convenience, and cost.

A capillary electrometer may be used in place of the galvanometer. It is a cheap, simple instrument to make, but not an easy instrument to use, for the movements of the mercury meniscus are very small and it is readily put out of commission by a relatively small electromotive force applied to it in the wrong direction Where it is used, it should be connected in such a way as to make the mercury side of the electrometer become more positive as the voltage changes during titration. This will reduce the danger of its becoming deranged

The inexpensive, portable "flip-flop" galvanometer,[1] though sensitive enough, is not always easy to use in a poorly lighted hood. A reflecting galvanometer placed outside the hood and arranged to throw a spot of light over the top of the operator's head onto a scale, or an index line on a white surface, behind the burets, makes an ideal arrangement. The box-type, lamp-and-scale galvanometers on the market[2] are also good; for, being entirely enclosed in a wooden box, they can be placed in the hood behind the burets with little danger that acid fumes will cause much damage.

Cost.

The material for either of the potentiometers of Fig. 1 and Fig. 2 can be bought for about $12. A portable galvanometer can be had for $18 or $20, and the reflecting type of galvanometer should not cost more than $50.

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[1] Such as the Leeds and Northrup Company's Type 2320 or the Weston Model 324.

[2] Such as the Leeds and Northrup Company's Type 2420.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA.]

THE VOLUMETRIC DETERMINATION OF HYDROXYLAMINE.

BY WILLIAM C. BRAY, MIRIAM E. SIMPSON AND ANNA A. MACKENZIE.

Received July 17, 1919

In the present investigation 3 volumetric methods of determining hydroxylamine in aqueous solution have been studied:

The titanous salt method,[1] in which the hydroxylamine is reduced by excess titanous salt in acid solution with exclusion of air, and the excess titrated with permanganate.

$$2NH_2OH + Ti_2(SO_4)_3 = (NH_4)_2SO_4 + 4TiOSO_4 + H_2SO_4. \quad (1)$$

The ferric salt method,[2] in which the hydroxylamine is oxidized in an acid solution by excess of a ferric salt, the mixture is boiled and the ferrous salt formed titrated with permanganate.

$$2NH_2OH + 2Fe_2(SO_4)_3 = N_2O + 4FeSO_4 + 2H_2SO_4 + H_2O. \quad (2)$$

The iodine method,[3] in which the hydroxylamine is oxidized by iodine in a neutral solution, *e. g.*, in the presence of disodium phosphate.

$$2NH_2OH + 2I_2 = N_2O + 4HI + H_2O \quad (3)$$

or

$$2NH_2OH + 2I_3^- = N_2O + 6I^- + 4H^+ + H_2O.$$

Our first experiments, with the iodine method, yielded irregular results which could not be interpreted until the concentration of the hydroxylamine solution was accurately determined. An examination of the literature showed a rather unsatisfactory state of affairs. The advocates of the ferric sulfate method furnish evidence that it is perfectly reliable, but Leuba[4] gives detailed experimental data to prove the contrary, and Adams[5] states that he could not obtain reproducible results with it. The investigators who have used the iodine method consider it to be fairly satisfactory, but some of them state that it is not very accurate, and Rupp and Maeder[6] have recently concluded that correct results are obtained only by a compensation of errors. Accordingly a study of various methods of standardizing an hydroxylamine salt solution was undertaken.

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[1] A. Staehler, *Ber.*, 37, 4732 (1904), 42, 2695 (1909).

[2] W. Meyeringh, *Ibid.*, 10, 1942 (1877); F. Raschig, *Ann.*, 241, 191 (1887); *Z. angew. Chem.*, 17, 1411 (1904); Ebler and Schott, *J. prakt. Chem.*, [2] 78, 320 (1908); Rupp and Maeder, *Arch. Pharm.*, 251, 297 (1913); Sommer and Templin, *Ber.*, 47, 1226 (1914).

[3] W. Meyeringh, *Ber.*, 10, 1940 (1877); T. Haga, *J. Chem. Soc.*, 51, 794 (1887); M. Adams, *Am. Chem. J.*, 28, 198 (1902); A. W. Stewart, *J. Chem. Soc.*, 87, 410 (1905); Petrenko-Kritschenko and Kantacheff, *Ber.*, 39, 1453 (1906); Acree and Johnson, *Am. Chem. J.*, 38, 316 (1907); Barrett and Lapworth, *J. Chem. Soc.*, 93, 85 (1908).

[4] Leuba, *Ann. chim. anal. appl.*, 9, 246 (1904)

[5] Adams, *Am. Chem. J.*, 28, 198 (1902).

[6] Rupp and Maeder, *Arch. Pharm.*, 251, 295 (1913).

The ferric salt and titanous salt methods were proved to be perfectly concordant.[1] Since the one method depends upon the oxidation of hydroxylamine to nitrous oxide and the other upon its reduction to NH_4^+ it follows that both methods must be accurate. The task of comparison was simplified by the fact that the results of both methods of analysis were obtained for the same solution of hydroxylamine sulfate and were referred to the same permanganate solution; possible errors in the calibration of pipets and burets and in the standardization of the reference solution were thus eliminated.

The Titanous Salt Method.

The use of an acid solution of a titanous salt as a standard reducing agent[2] deserves more attention than it appears to have received. The necessary precaution of excluding the oxygen of the air from the stock solution and during titrations is easily taken by means of carbon dioxide gas, and the preparation of the stock solution by reducing a titanium salt solution is not a very difficult task.

A solution of titanium sulfate, approximately 0.1 molar, and containing 5% of sulfuric acid, was prepared by dissolving titanium dioxide in conc. sulfuric acid and diluting to the proper volume. This was reduced by the method of Van Brunt[3] in a 20-inch Jones reductor heated electrically by a resistance coil which surrounded the lower part of the reductor tube. The reductor was half filled with amalgamated granular zinc which was kept covered with 5% sulfuric acid when not in use Reduction was rapid at a temperature below the boiling point, and the purplish black color showed the progess of the reduction. The wide upper end of the reductor was closed with a rubber stopper fitted with a dropping funnel to hold the solution, and with a vent which could be closed to force the reduced solution into the container. Through the latter a current of carbon dioxide was passed.

A 75 to 100 cc. portion of titanium sulfate solution was reduced in each operation. Time was saved by warming the solution before introducing it into the reductor, and 15 to 20 minutes was then sufficient for each treatment. With a little practice, a liter of solution can be reduced in 4 hours. One difficulty must be noted: the solution should not be boiled either before or during reduction, since a precipitate may then form. On this account no attempt was made to completely reduce the titanium in the solution.

The titanous sulfate solution (approximately 0.1 *N*) was shaken and allowed to stand several hours before being used. The solution when needed was siphoned into a buret filled with carbon dioxide; the tip of the buret was inserted through a rubber stopper into an Erlenmeyer titration flask; carbon dioxide was passed into the flask and escaped through the hole in the cork into which the buret tip was inserted. The container and the top of the buret were permanently connected with the carbon dioxide supply.

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[1] This result is in agreement with Staehler's conclusion from two analyses, one by each method, which differed by only 0.5%; A Staehler, *Ber.*, 37, 4732 (1904).

[2] Treadwell-Hall, *Quant. Anal.*, 1912, pp. 699–701; Knechtand Hibbert, *Ber.*, 36, 1549 (1903), 38, 3318 (1905).

[3] Van Brunt, THIS JOURNAL, 36, 1426 (1914).

The concentration of the solution was determined, just before use with hydroxylamine, by means of 0.1 *N* potassium permanganate solution, which had been standardized against Bureau of Standards sodium oxalate. In each titration 20 to 25 cc. solution was run into the titration flask, the buret tip was slipped out of the hole in the rubber stopper, the tip of the permanganate buret inserted, and the potassium permanganate added at once to a faint pink.

The hydroxylamine solution was analyzed as follows: 10 cc. approximately 0.2 *N*, or 20 cc. 0.1 *N*, hydroxylamine was placed in the titration flask; about twice the theoretical amount of titanous sulfate was added from the buret; after 8 to 10 minutes the excess was titrated with the permanganate solution.

Two titanous sulfate solutions were prepared. Each was standardized on the day the corresponding hydroxylamine results given below were obtained:

First solution, 0.09887 *N*, 0.09893 *N* Average, 0.0989 *N*.
Second solution, 0.1056 *N*, 0.1058 *N*, 0.1057 *N* Average, 0.1057 *N*.

It follows that the titanous sulfate-permanganate titration is reproducible to 0.1 or 0.2%.

Four consecutive hydroxylamine determinations, made with the aid of the first titanous sulfate solution, yielded the following results:

10.00 cc. of NH_2OH solution is equivalent to 18.62, 18.69, 18.69, 18.61 cc. of 0.1 *N* $KMnO_4$

Concentration of NH_2OH, calculated from average, 0.1864 *N*.
Concentration of NH_2OH, by ferric sulfate method, see below, 0.1865 *N*.

Another set of results with a different hydroxylamine sulfate solution was obtained with the second titanous sulfate solution.

20.00 cc of NH_2OH solution is equivalent to 21.48, 21.62, 21.62, 21.77 cc. of 0.1 *N* $KMnO_4$.

Concentration of NH_2OH, calculated from average, 0.1081 *N*.
Concentration of NH_2OH, by ferric sulfate method, see below, 0.1081 *N*.

The individual determinations of hydroxylamine by the titanium method agree within a few tenths of per cent., and therefore, as will be seen later, this method is as satisfactory as the ferric sulfate method. The agreement of the average values from the two methods is better than was to be expected, and furnishes a definite proof of the correctness of both methods.

The Ferric Salt Method.

Dilute solutions of hydroxylamine sulfate were analyzed as follows: 10 cc. of approximately 0.2 *N* hydroxylamine (or 20 or 25 cc. of approximately 0.1 *N* strength) were pipetted into a 400 cc. Erlenmeyer flask which contained 50 cc. of ferric sulfate solution (40 g. of $Fe_2(SO_4)_3.9H_2O$ per liter) and 15 cc. of sulfuric acid (approximately 12 *N*); the mixture was boiled vigorously for 5 minutes, cooled, made up to about 200 cc. with water and titrated with 0.1 *N* permanganate solution.

The results obtained with one solution follow:

10.00 cc. of solution, 18.84, 18.39, 18.43, 18.61, 18.61 cc of 0.1 *N* $KMnO_4$ (concentration, from average, 0.1860 *N* NH_2OH).

After 3 weeks, 18.59, 18.69, 18.64 cc (average, 0.1864 *N* NH_2OH)

After 6 weeks, 18.63, 18.69, 18.64 cc (average, 0.1865 *N* NH_2OH)

Equally satisfactory results were obtained with other solutions. It is evident that the results are reproducible to within a few tenths of a per cent. and that the hydroxylamine sulfate solution undergoes little, if any, change of concentration over a considerable period of time.

In the above experiments the hydroxylamine solution was added to the ferric sulfate-sulfuric acid solution at room temperature, and a few minutes elapsed before the solution could be heated to boiling. The following data show that the result is not appreciably altered when the hydroxylamine is added to a boiling solution

20.00 cc of NH_2OH solution, usual method, 21.62, 21.65, 21.62, 21.60 cc. of 0.1 *N* $KMnO_4$ (concentration, from average, 0.1081 *N* NH_2OH)

20.00 cc of NH_2OH solution, added to a boiling $Fe_2(SO_4)_3$ solution, 21.72, 21.66 cc.

The time of vigorous boiling may be made longer than 5 minutes. One experiment in which this time was 20 minutes agreed with the reference experiments within 0.4%.

The already large excess of ferric salt (about 3-fold) may be greatly increased. In one experiment in which 3 times the usual volume of ferric sulfate solution was added the result was unchanged.

The presence of ammonium salts in large amount does not affect the results, and the ferric sulfate can be replaced by ammonium iron alum. One of several series of results with 10.00 cc. of hydroxylamine sulfate solution, 40 cc of a solution of ammonium iron alum saturated at room temperature, and sulfuric acid is given.

18.67, 18.67, 18.67, 18.68 cc of 0.1 *N* $KMnO_4$

The average of a series with ferric sulfate instead of the iron alum (18.62 cc.) agreed with these results within 0.3%.

The conditions outlined above for the analysis are those originally recommended by Raschig, *viz.*, the large excess of ferric salt, the boiling, and the presence of acid. Our results thus confirm the work of those who endorsed the method, and disprove the criticisms of Adams. Of the detailed results of Leuba only one was obtained under the conditions recommended, and this discordant result must be rejected.

That errors will result when the analysis is made under other conditions was pointed out by Raschig. He emphasized especially the large error that will be made if the permanganate is added before the reaction (Equation 2) is completed: too much potassium permanganate is then used, and nitrogen is oxidized beyond the nitrous oxide stage Leuba's results (except the one referred to in the preceding paragraph) illustrate the magnitude of this error, *e. g.*, 55% and 30% excess permanganate was required after the hydroxylamine, excess ferric alum, and sulfuric acid had been digested for $^3/_4$ hour at 26° and 82°, respectively.

If the permanganate is added while hydroxylamine is still present an error of this kind will result. Raschig[1] investigated this reaction in the presence of sulfuric acid (and absence of ferric sulfate); the amount of permanganate varied from about 2 to 1.5 times that necessary to form nitrous oxide, while the temperature of the hydroxylamine solution was varied between room temperature and 100°. Raschig accordingly rejected the permanganate method of analysis.[2]

With regard to the reaction between hydroxylamine and excess ferric sulfate Raschig[3] *concluded that the hydroxylamine was rapidly used up*, and that the positive error was due mainly to the presence of an intermediate substance, nitroxyl, NOH,—which was completely transformed into nitrous oxide by the 5-minute boiling The recent work of Angeli[4] furnishes additional evidence in favor of nitroxyl as a possible intermediate step; but the existing evidence is scarcely sufficient to enable us to determine just when the positive error is due to reaction of potassium permanganate with hydroxylamine and when due to nitroxyl. That it is not due to a reaction between potassium permanganate and nitrous oxide we found by a direct experiment.

While the necessity of boiling the solution had thus been demonstrated, we did not find quantitative data with regard to the errors that might result from a variation of the concentrations of acid and ferric sulfate. To obtain this information the following experiments were performed in this laboratory by Dr. H. E. Miller.

Effect of Varying Concentration of Acid.—The experiments listed below followed the standard precedure: the volume noted in the fifth volumn is the volume of solution boiled for 5 minutes. Dilution to 200 cc. after cooling was found to have no effect on the amount of permanganate used in the titration.

[1] Raschig, *Ann.*, 241, 188 (1887).

[2] In spite of this warning the method has been used Cf. Patten and McCaughey, *Trans Am. Electrochem. Soc*, 15, 544 (1909).

[3] Raschig, *Z. angew. Chem.*, 17, 1411 (1904).

[4] Angeli, *Ahrens' Sammlung*, 13, 1 (1908).

No.	Cc ferric sulfate.	Cc. 12 N H_2SO_4.	Volume. Cc.	Cc. $KMnO_4$.			Titration result, % theoretical.
Using 25 cc. of Hydroxylamine Solution.							
1	50	15	90	23.0,	23.05,	23.0	100%
2	50	15	101	23.0,	22.95,	...	100%
3	50	7.5	86	22.95,	23 0	22.90	99.8%
4	25	4	101	22.90,	...	...	99.6%
5	50	2	75	22.74	...	...	98.9%
6	25	1	75	22 60,	22 65	..	98.4%
7	50	0	100	22.23	...	..	96.6%
8	50	NaAc	100	22 20	...	...	96.5%
Using 10 cc. of Hydroxylamine Solution.							
9	25	0	75	8.85	..	...	96 2%
10	25	NaAc	75	8.85,	8.92	...	96.6%

These results show that a lowering of the concentration of the sulfuric acid produces a negative error. The error is negligible when the amount of acid used is half that recommended in the standard procedure, but may be as large as 3 or 4% when no acid is used. Expts. 8 and 10 were duplicates of 7 and 9, respectively, except that sodium acetate was added initially to the ferric sulfate solution in order to keep the hydrogen ion concentration low during the reaction. However, although the acid formed in the reaction made the hydrogen ion concentration higher in Expts. 7 and 9, the results were practically the same as in Expts. 8 and 10.

After some experimentation this negative error was found to be due to the oxidation of ferrous salt by oxygen of the air. This reaction occurs mainly during the first stage of the operation while the solution is being heated from room temperature to the boiling point. In an acid solution at room temperature in 1 hour there is no appreciable oxidation of ferrous sulfate solution in contact with air.

Some of the above experiments were repeated in an atmosphere of carbon dioxide (which contained only about 0.1% oxygen); the ferric sulfate solution was boiled to expel the air and cooled under carbon dioxide, the hydroxylamine was added, the mixture was boiled for 5 minutes, some sulfuric acid was added, the mixture was again boiled, and cooled under carbon dioxide. The apparatus consisted of an Erlenmeyer flask closed with a 3-hole rubber stopper, fitted with an inlet and outlet for carbon dioxide and a separating funnel (with stopcock) for introducing the hydroxylamine. The experiments are numbered to show the relation to the corresponding experiments in the first table.

Experiments in an atmosphere of carbon dioxide.

3(*b*), Vol. = 100 cc.: 23.02, 23.0, 22.95 cc. $KMnO_4$ (100% instead of 99.8%).
5(*b*), Vol. = 100 cc.: 22.92 (99.7% instead of 99.6%).
7(*b*), Vol. = 100 cc.: 22.65, 22.64, 22.68, 22.82 (98.6–99.2% instead of 96.6%).

In these experiments the error was greatly reduced; and, since the elimination of air could scarcely have been complete, it seemed probable that the negative error was due solely to the oxygen in the air.

Finally we tried the elimination of this error by the simple method of boiling the ferrous sulfate solution to expel the air, and introducing the hydroxylamine into the boiling solution from a pipet. Otherwise the experimental conditions were the same as in Expt. 7.

No. 7(*c*), Vol. = 75 cc.: 23.0, 23.0 cc. $KMnO_4$, 100%.

There are therefore two satisfactory methods of preventing an error due to the oxidation of the ferrous salt by oxygen of the air:

(1) by the use of the regular procedure; the hydroxylamine is added at room temperature to excess ferric sulfate in a solution which is 2 to 3 normal with respect to sulfuric acid;

(2) by adding the hydroxylamine slowly to a boiling ferric sulfate solution.

Effect of Varying Ferric Sulfate Excess.—The experiments listed below were performed by the regular procedure. The ferric sulfate was much less than the usual amount, except in Expts. 11, 12 and 13. The amount is shown in the third column as number of equivalents in terms of the hydroxylamine used. Thus 1.40 means that the amount of ferric sulfate was 40% greater than the theoretical amount necessary to oxidize hydroxylamine to nitrous oxide; 25 cc. of ferric sulfate was in theory sufficient to oxidize 38.4 cc. hydroxylamine solution. It is to be noted that in Expts. 21–25 the amount of acid was much less than usual.

No	Ferric sulfate referred to NH_2OH.	Cc 12 *N* H_2SO_4	Volume Cc.	Cc $KMnO_4$.	Titration result, % theoretical.
	Using 25 cc. of Hydroxylamine Solution.				
11	2.95	15	90	23.0, 23.05, 23.0	100%
	Using 10 cc. of Hydroxylamine Solution.				
12	3.84	7.5	65	9.2, 9.2	100%
13	2.92	15	65	9.2, 9.1	100%
14	2.33	15	65	9.2	100%
15	1.75	15	65	9.25, 9.25	100.5%
16	1.53	7.5	65	9.4	102%
17	1.45	15	65	9.45, 9.30	101 to 103%
18	1.40	8.5	50	11.3+	123+%
19[1]	1.40	8.5	50	9.6	104.4%
	Using 25 cc. of Hydroxylamine Solution.				
20	1.08	7.5	91	24.2, 24.8	105–108%
	Using 10 cc. of Hydroxylamine Solution.				
21	1.75	1	65	9.15, 9.15, 9.15	99.5%
22	1.75	1	65	9.1	99%
23	1.40	1	50	9.1, 9.05	98.8%
24[1]	1.40	1	50	9.1	99%
	Using 25 cc. of Hydroxylamine Solution.				
25	1.08	2	80	23.6	102%

[1] In Expts. 19 and 24 the time of boiling was 30 minutes instead of 5 minutes.

Expts. 15 to 20 furnish clear evidence of a positive error when only a small excess of ferric sulfate is used. The results are irregular when only

40% or less excess ferric salt is used, and in one experiment (18) the permanganate end-point was not definite; in this case the titration was discontinued before a permanent color was obtained. In the companion experiment (19) with 30 minutes' boiling instead of 5 minutes the end-point was permanent. It was found by experiment that fleeting end-points (and high positive errors) were characteristic for experiments in which the reaction mixture was not heated, or was heated only to boiling. The error due to the small excess of ferric salt, therefore, is similar in character to that due to insufficient boiling in the standard procedure, and is doubtless due to the presence of hydroxylamine or nitroxyl when the permanganate is added. (See discussion earlier in paper.)

The results in Expts. 21 to 25, where the concentration of acid also is low, are more nearly correct; but this may be due to a compensation of the positive error resulting from incompleteness of the reaction and the negative error due to oxygen (which is favored by a low concentration of acid). To obtain further evidence the following experiments were performed in which the oxygen error was eliminated by adding 25 cc. of hydroxylamine solution from a pipet to the boiling ferric sulfate solution, as in Expt. 7(*c*). In Expts. 27 and 28, while no acid was added initially, in order that the permanganate titration might be made satisfactorily, 6 cc. of 6 *N* sulfuric acid was added to the hot solution after 5 minutes' boiling and just before the rapid cooling.

No	Ferric sulfate referred to NH_2OH.	Cc. 12 *N* H_2SO_4	Volume Cc.	$KMnO_4$. Cc.	Titration result, % theoretical.
		Using 25 cc. of Hydroxylamine Solution.			
26	1.45	15	80	27.1	117%
27	1.45	0	75	22.95	99 8%
28	1.16	0	75	22.9	99.6%

The slight negative error in Expts. 27 and 28 indicates that the oxygen error was not quite completely eliminated, but they serve to show that the positive error is negligible when the ferric sulfate excess is small provided that the sulfuric acid concentration also is small. In other words, a high concentration of sulfuric acid retards the reaction, and the reaction can be completed in 5 minutes' boiling only when a very large excess of ferric sulfate is used. This conclusion is confirmed by the result of Expt. 26.

With regard to the relative merits of the two methods of making the ferric sulfate analysis, listed at the end of the preceding section, we are inclined to favor the first one, the regular procedure, since it has been more thoroughly tested. Also as noted in the preceding paragraph there seems to be a slight tendency towards a negative error in the second method.

Effect of the Presence of Chloride Ion.—While hydroxylamine sulfate was used throughout our experiments, it is certain that the ferric sulfate method is equally applicable to the analysis of hydroxylamine hydrochloride. Permanganate is not added until the final solution has been cooled and diluted, and the concentration of chloride ion will then be so small that there can be no appreciable reaction to form chlorine. Raschig's original experiments to test the method of analysis were made with hydroxylamine hydrochloride, and we also found that the addition of an amount of hydrochloric acid approximately equivalent to the hydroxylamine made no appreciable difference in the result.[1]

Analysis of the Gas Formed in Reaction 2.—At an early stage in this investigation, while we were still uncertain that hydroxylamine was quantitatively oxidized by the ferric ion to nitrous oxide, Mr. G. S. Parks undertook the analysis of the gas involved. He constructed an apparatus which enabled the hydroxylamine solution and the ferric sulfate-sulfuric acid solution to be mixed after the apparatus had been evacuated. Gas was evolved only very slowly at room temperature, but rapidly when the solution was heated to boiling. The gas was analyzed by adding excess hydrogen, burning and measuring the contraction; then adding excess oxygen, burning and measuring the contraction; absorbing the oxygen and measuring the residual nitrogen. The gas was found to be pure nitrous oxide within the experimental error. Three complete analyses gave 98.1, 99.9 and 100.0% nitrous oxide; a fourth analysis, based solely on the contraction with hydrogen, gave 101% nitrous oxide.

The Iodine Method.

The reaction between iodine and hydroxylamine in aqueous solution, as earlier investigations have shown, is rapid at low hydrogen ion concentration, *e. g.*, in the presence of sodium hydrogen carbonate or disodium phosphate. The rate is extremely slow in the presence of acid. Thus when 0.1 *N* iodine solution (in potassium iodide) was added drop by drop to 10 cc. of 0.1 *N* hydroxylamine sulfate solution, three drops (0.10 cc.) gave a color which persisted for several minutes; the minute amount of acid formed in the reaction with this amount of iodine gave a sufficient concentration of hydrogen ion practically to stop the reaction. In another experiment in 72 cc. of solution containing disodium phosphate and phosphoric acid in the proportion of 2 : 1, 0.06 cc. of iodine solution gave a distinct color When in each of these experiments excess disodium phosphate solution was added, iodine was rapidly used up. Even in the phosphate solution, however, the reaction was not instantaneous near the end-point. On this account, after the preliminary experiments, the end-point was usually obtained by adding iodine solution in excess, usually about 5 cc. and after 3 to 5 minutes completing the titration with thiosulfate solution.

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[1] Cf the recent experiments on the effect of the presence of chloride in the determination of nitrite by permanganate, Laird and Simpson, THIS JOURNAL, 41, 530 (1919).

To remove the hydrogen ion formed in the reaction a phosphate solution was used which contained in one liter 0.1 mol of disodium phosphate and enough phosphoric acid to make the solution colorless when tested with phenolphthalein; the ratio of disodium phosphate to sodium dihydrogen phosphate in the solution was about 10 to 1. By using 200 cc. of this solution with 20 to 25 cc. of 0.1 *N* hydroxylamine sulfate the ratio of the monohydrogen and dihydrogen phosphates in the final solution was made about 2 : 1. Under these conditions there is no danger either of iodate formation, or of incomplete oxidation of hydroxylamine.

In our first experiments, even after elimination of the low results due to incomplete reaction (in the presence of too much acid), the results were extremely variable, the extremes differing by over 15%. As reported by other investigators, many factors were found to influence the results. When the total volume of the solution was large the results were relatively high, as Haga has pointed out. Increase of the concentration of iodide ion by the addition of potassium iodide tended to lower the results, although Haga had found that the presence of neutral salts, as sodium sulfate, caused high results. Increase of temperature, in the case of incomplete reaction, caused the reaction to proceed towards completion and thus raised the result; in other cases, however, low temperature seemed to favor high results. A very important factor was the method of adding the phosphate and iodine solutions,—including the order of mixing, and the time allowed. The results were very high when the phosphate and hydroxylamine solutions were mixed and the titration made by adding iodine to the mixture. Much lower results were obtained when the end-point was approached from the acid side, *e. g.*, by mixing iodine and hydroxylamine and gradually adding the phosphate solution, or by adding the iodine and phosphate solutions alternately.

When the hydroxylamine solution was accurately standardized by the two methods already described in this paper, and the theoretical results for the iodine titration compared with the actual data, it was found that the results described in the preceding paragraph as relatively high were definitely in error. For example, when 200 cc. of phosphate solution and 10 cc. of hydroxylamine solution were mixed at room temperature before any iodine was added, two determinations gave 21.33 and 21.22 cc. of 0.1 *N* iodine solution, while the theoretical result was 18.64 cc. Positive errors were the rule rather than the exception, at least when precautions were taken to ensure completeness of reaction.

The only definite source of error already known is nitrite formation, demonstrated by Haga. Since this involves oxidation of the nitrogen beyond the nitrous oxide stage, too much iodine must be used, and a positive error results. The conditions described above as favoring high results thus presumably favor nitrite formation.

We next developed an *empirical method* which gave theoretical results. To the hydroxylamine solution in an Erlenmeyer flask was added an excess of 0.1 *N* iodine solution from a pipet or buret; 40 cc. of phosphate solution was added from a buret in 5 cc. portions at 2-minute intervals and then the remaining 160 cc. of phosphate solution was added; after 5 minutes the excess iodine was titrated with 0.1 *N* thiosulfate solution. It was observed that the reaction between hydroxylamine and iodine was nearly completed by the time the 40 cc. of phosphate solution had been added. In one set of experiments with 10 cc. of 0.1864 *N* hydroxylamine solution, while the theoretical result was 18.64 cc. of 0.1 *N* iodine solu ion, the following results were obtained: 18.78, 18.56, 18.58, 18 71, 18.66, 18.60 and 18.46 cc. of 0.1 *N* iodine solution. Thus the results are reproducible, but only when the prescribed conditions are maintained.

The question arose as to whether this method gave correct results only because there was a compensation of errors. Direct evidence was finally obtained by determining accurately the amount of nitrite in the final solution. Nitrite was always found; and since this implies a positive error there must have been an as yet undiscovered compensating negative error.

The method used in the *determination of nitrite* in the presence of phosphate and iodide was that developed independently by Chabrier[1] and by Raschig[2] which has recently been tested by Davisson.[3] It depends upon the fact that nitrite does not react with iodide in neutral solution, but is quantitatively reduced to nitric oxide in the presence of acid; the liberated iodine is titrated with thiosulfate solution after 2 minutes. Air is excluded by means of carbon dioxide, since otherwise nitric oxide would react with oxygen, the product would be reduced by iodide, and the formation of iodine would continue due to continued repetition of this cycle. The presence of nitrous oxide has no effect since nitrous oxide does not oxidize iodide ion in acid solution.

In analyses made by the empirical method with 25 cc. of hydroxylamine sulfate solution, the theoretical value is 25.16 cc. of 0.1 *N* iodine solution, but the final solution was found to contain enough nitrite to liberate 0.60 to 0.70 cc. of iodine when the nitrite was reduced to nitrous oxide. This would correspond to a positive error in the iodine titration of 1.2 to 1.4 cc. of 0.1 *N* iodine solution (the amount being doubled since the theoretical result is based on the quantitative formation of nitrous oxide), which is an error of about 5%.

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[1] Chabrier, *Encyclopédie chimique*, 4, 262 (1888); see Wiley, *Princ. and Pract. of Agric. Anal.*, 2nd Ed., II, 474 (1908)

[2] Raschig, *Ber.*, 38, 3911 (1905)

[3] Davisson, THIS JOURNAL, 38, 1683 (1916).

The final solution after the iodine titration might also contain nitroxyl, and it was therefore necessary to devise a method of eliminating this substance. From Raschig's work and our own experiments with the ferric sulfate method it seemed certain that this could be done by boiling the final solution. The effect of boiling on the nitrite method was accordingly determined. It was found that a mixture of nitrite, iodide, and 200 cc. phosphate solution could be boiled for 5 minutes without appreciable loss of nitrite. However, when a solution containing tetrathionate, iodide, and phosphate was boiled an appreciable amount of a reducing agent was formed, and the quantity continued to increase with continued boiling. The reducing agent was determined by titration with iodine; after several hours' boiling the formation of reducing agent was still continuing, although the amount of iodine that had been used was over twice that necessary to form the original amount of tetrathionate from thiosulfate; no sulfur was precipitated.

Since it was evidently impossible to boil any final solution (after the iodine titration of hydroxylamine) which contained tetrathionate, some experiments were performed in which sulfurous acid was used instead of thiosulfate. The sulfurous acid titration was the basis of the original Bunsen method of determining iodine, and is reliable provided the sulfurous acid solution is standardized each day before use. However, the titration was found to be unreliable in the presence of our phosphate solution; too much sulfurous acid was used, and errors of more than 10% were observed. When the phosphate solution, after this titration, was boiled for 5 minutes no reducing agent was formed. Accordingly sulfurous acid was used simply to remove the excess of iodine in the hydroxylamine determination; analyses were made by the empirical method, with 25 cc. of hydroxylamine solution as in the experiments described in the preceding paragraph; the final solution was boiled for 5 minutes, and cooled under carbon dioxide, the amount of nitrite was found to be practically the same as before. It follows that, in the empirical iodine method for determining hydroxylamine, nitrite is formed corresponding to a positive error of about 5%, and that there must be a compensating negative error.

Before describing our final experiments the results of a number of experiments will be described in which the final solution after the iodine titration was acidified with sulfuric acid in the presence of air. The same behavior was observed as in blank experiments with nitrite in the presence of the phosphate solution, the formation of iodine was rapid at first and was continuing only very slowly after 24 hours. In the experiments by the empirical method, similar to those in which nitrite was determined, after 24 hours the amount of iodine liberated in the acidified solution was equal to 10 to 16 cc. of 0.1 *N* iodine. This was not greater than was to be expected for the amount of nitrite known to be present. Also when the solution was again made approximately neutral by the addition of a large amount of solid disodium phosphate, hydroxylamine was found to be absent. There is therefore no evidence that the formation of nitroxyl from hydroxylamine by means of iodine is a reversible reaction. Before the nitrite experiments were performed we had thought that the large amount of iodine formed on the addition of acid was due, in part at least, to a reaction between nitroxyl, iodide ion and hydrogen ion.

The negative error referred to in the paragraphs just before the preceding one was proved to be due to the presence of oxygen of the air. This error appears to be absent when the hydrogen ion concentration is very low throughout the reaction between hydroxylamine and iodine, *e. g.*, when the phosphate solution is added before the iodine. Any nitrite formed remains in the solution unchanged, since it cannot react with iodide ion under these conditions. On the other hand, this error is encountered when the phosphate solution is added slowly to the hydroxylamine-iodine solution, as in the empirical method. It seems probable that the hydrogen ion concentration is then large enough to permit of some reaction between the nitrite and iodide, the nitric oxide formed is oxidized by oxygen and the product is reduced, with the result that some iodine is liberated due to the presence of oxygen. According to this theory the correctness of the empirical method depends upon the time allotted for the addition of the phosphate solution, and it is to be predicted that low results will result if this time is increased. The following experiments were performed by the empirical method of analysis, except that in the second and third experiments, after 30 cc. of phosphate solution had been added, the mixture was allowed to stand in contact with air for 1 and 12 hours, respectively.

25 cc. of Hydroxylamine Solution = 23.16 cc. of 0.1 *N* Iodine Solution.

Time of interruption after addition of 30 cc. phosphate	Result of titration. Cc. of 0.1 *N* iodine solution	Nitrite determination. Cc. of 0.1 *N* iodine solution
2 min.	23.2	0.7
1 hour	22.1	0.6
12 hours	21.0	0.25

The results, in the second column, are distinctly low in the second and third experiment, as was expected. It is interesting to note that the nitrite also decreased with time, which also favors the theory outlined above. Two additional experiments were performed by the empirical method but in the presence of carbon dioxide. In the first experiment, in which the air was only partially eliminated, the final result was 23.3 cc. of 0.1 *N* iodine solution, and the nitrite determination 0.6 cc. of iodine solution. In the second experiment, where the exclusion of air was more satisfactory, the final result was 23.5 cc. of iodine solution, and nitrite 0.55 cc. of iodine solution. Thus when the amount of air is decreased the titration results are somewhat higher.

The iodine method therefore seems to be of little value. The empirical method gives correct results only on account of a compensation of the positive error due to nitrite by the negative error due to oxygen. Nitrite is formed under widely different conditions, and it seems scarcely worth while to continue the search for conditions in which the oxidation to nitrous oxide will be quantitative.

Reaction of Iodine and Thiosulfate in Disodium Phosphate Solution.

As a result of the observation of the instability of tetrathionate in the hot phosphate solution, referred to above, some experiments were performed on the reaction between iodine and thiosulfate in the presence of phosphate. It is recalled that our disodium phosphate solution contained a small proportion of sodium dihydrogen phosphate.

When the iodine-thiosulfate titration was made in this solution at room temperature an error of about 1% was observed, in the direction that too much iodine was used.[1] This error was eliminated if enough acid was first added to the phosphate solution to convert the disodium phosphate into a mixture of sodium dihydrogen phosphate and phosphoric acid. It is to be noted that in the hydroxylamine determination, since thiosulfate was used to determine the small excess of iodine added, a slight positive error was thereby introduced. It was negligible, however in comparison with the large positive error due to nitrite.

Three experiments on the reaction between iodine and thiosulfate in disodium phosphate solution at a higher temperature were made for us by Miss Jennie Clauson in this laboratory. 8.8 cc. of 0.1 *N* thiosulfate solution, somewhat more than an eightfold amount of iodine in potassium iodide solution, water, and 18 g. of $Na_2HPO_4.12H_2O$ were placed in 100 cc. Pyrex glass tubes, the tubes were sealed and heated at 70 to 90° in a water-bath for about one hour. The excess iodine was determined at room temperature by titration with thiosulfate.

Expt. No.	1.	2.	3.
Temperature (approx.)	70°	70°	90°
	Cc. Thiosulfate Solution Equivalent.		
Iodine solution	79.6	79.6	79.6
Iodine excess	10.5	10.55	8.6
Iodine used	69.1	69.05	71.0
$^1/_8$ iodine used	8.64	8.63	8.87
Thiosulfate solution used	8 8	8.8	8.8

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[1] That iodate was not formed was proved by acidifying the final solution with H_2SO_4; there was no liberation of iodine at once.

Within the limits of the experimental error the amount of iodine used is 8 times that required to oxidize the thiosulfate to tetrathionate. It is obvious that there is quantitative oxidation to sulfate.

$$S_2O_3^{--} + 4I_2 + 5H_2O = 2SO_4^{--} + 8I^- + 10H^+.$$

While the corresponding reactions with excess bromine and chlorine are well known, we have as yet found no reference to this reaction for iodine.

Quantitative Oxidation of Hydroxylamine to Nitrate.

The work of Knorre and Arndt[1] shows the scarcity of quantitative reactions when hydroxylamine is treated with oxidizing agents. On this account it is interesting to note that Rupp and Maeder[2] have recently demonstrated the quantitative oxidation of hydroxylamine to nitrate in acid solution by excess of a bromate-bromide mixture or of a hypobromite-bromide mixture. Since bromine can be formed in both cases it seems certain that bromine will have the same effect.

Early in the present investigation we made a few experiments on the reaction between hydroxylamine and hypochlorous acid, the latter in small excess over that necessary for oxidation to nitrate assuming reduction of hypochlorous acid to chlorine. Precautions were taken to prevent loss of chlorine, and the total amount of oxidizing agent that remained after a few minutes was determined by adding potassium iodide and titrating the iodine formed with thiosulfate. The amount of hypochlorous acid used in this reaction was found to vary between 90 and 97% of that calculated for oxidation of hydroxylamine to nitrate. It seems not improbable that conditions could be found in which this reaction would be quantitative, but we have not had an opportunity to continue these experiments.

Summary.

Three methods for the determination of hydroxylamine have been investigated: (1) the reduction of hydroxylamine to ammonium salt by excess titanous salt in acid solution, (2) the oxidation to nitrous oxide by excess ferric sulfate in sulfuric acid solution, with titration of the ferrous salt by permanganate solution, and (3) the oxidation to nitrous oxide by iodine in a solution kept neutral by means of sodium monohydrogen phosphate.

The titanous salt and ferric salt methods were found to be accurate, but the iodine method was unsatisfactory.

In addition to the known positive error in the ferric salt method, which is due to the addition of permanganate while some hydroxylamine or an intermediate product, nitroxyl, is still present, a negative error due to oxygen of the air was found under certain conditions. Both errors are easily avoided.

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[1] Knorre and Arndt, *Ber.*, 33, 30 (1900).

[2] Rupp and M aeder, *Arch. Pharm.*, 251, 298 (1913).

In the iodine method three errors were encountered: (1) that due to incomplete reaction, which is avoided by the addition of disodium phosphate, (2) nitrite formation which occurs under all the conditions investigated and corresponds to a positive error, and (3) absorption of oxygen of air, which corresponds to a negative error. An empirical method was developed for obtaining theoretical results, but it was shown to be correct only on account of compensation of errors (2) and (3).

Hydroxylamine is oxidized mainly to nitrate by hypochlorous acid solution in excess.

In a disodium monohydrogen phosphate solution thiosulfate can be oxidized quantitatively to sulfate by iodine. The reaction is rapid at 70°.

BERKELEY, CALIFORNIA

NOTES.

Corrections.—"*A New Theory Relating Constitution to Taste.*" The following corrections should be made in the article which appeared under this title in the June issue:[1]

P. 859, first formula on third line, $CO_2H.CHNHCH_3$-(H), and first formula on 5th line, $CH_2OH.CH_2.CHOH$-(H). The (H) should be omitted in both cases.

P. 859, in line 7, formula CHONO-(H) should read CH_2ONO-.

P. 860, classification of auxoglucs. Formula given under (3), C_nH_{2n+10} should read $C_nH_{2n+1}O$, and formula under (4), C_nH_{2n+10n} should read $C_nH_{2n+1}O_n$.

P. 861, formula of serine, $CH_3OH_2CHNH_2CO_2H$, should read $CH_2OH.$-$CHNH_2.CO_2H$.

P. 663 and 664. In Tables I, II and III, last line, the formula of the auxogluc should read in each case $C_nH_{2n+1}O_n$.

P. 867, under (2) the fifth formula, $C^{H_{1-x}}_{HI_x}$—, should read $C^{H_{1-x}}_{H_{1x}}$—.

P. 867, (3), the first formula under (*b*), $C_nH_{2n+1}O$, should read C_nH_{2n+1}, and the first formula under (*d*), $C_nH_{2n-1}O_n$, should be $C_nH_{2n+1}O_n$.

ERNEST OERTLY,
ROLLIN G. MYERS.

Correction.—The omission of certain lines from Table III of my paper, in the July JOURNAL,[2] on "The Activities of the Ions of Strong Electrolytes" makes the material there presented difficult for a reader to interpret. The activity ratios (Cols. 9 and 10) refer to the pairs of concentrations of hydrochloric acid and potassium chloride given in Cols. 4 and 5. A correct version of the table appears below.

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[1] THIS JOURNAL, 41, 855 (1919).

[2] *Ibid.*, 41, 1089 (1919).

TABLE III.

Substance.	Type of cell.	Temp	Concentrations C₁	Concentrations C₂	E M F. of cell.	Trans No of cation.	Activity ratios a_1/a_2 for Cl⁻.	Activity ratios a_1/a_2 for H+	
HCl	B	18°	0.006686	0.001665	—0.05614	0.833	3.82	3.84	J.
KCl	B		0.006700	0.001670	—0.03330	0.495			J.
HCl	B	18°	0.008315	0.001665	—0.06487	0.833	4.70	4.74	J
KCl	B		0.008329	0.001670	—0.03844	0.495			J.
HCl	B	18°	0.01665	0.001665	—0.09235	0.833	8.86	9.38	J.
KCl	B		0.01670	0.001674	—0.05434	0.496			J.
HCl	B	18°	0.03330	0.003329	—0.09162	0.833	8.76	9.14	J
KCl	B		0.03347	0.003347	—0.05403	0.496			J.
HCl	A	25°	0.05	0.005	—0.11234		8.64	9.16	N. and E.
KCl	A		0.05	0.005	—0.11085	.....			M. and P
HCl	A	25°	0.1	0.01	—0.1116	.	8.33	9.23	N and E.
HCl	A		0.1	0.01	—0.1117				L. B. S.
KCl	A	25°	0.1	0.01	—0.1089				M. and P.
KCl	B		0.1	0.01	—0.0540	0.495			M. and P.

D. A. MACINNES.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY.]

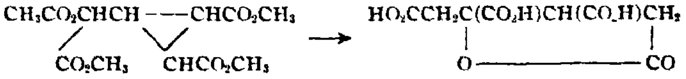
STUDIES IN THE CYCLOPROPANE SERIES.

VII. NITROCYCLOPROPANES.

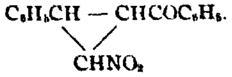
BY E. P. KOHLER AND H. F. ENGELBRECHT.

Received May 31, 1919

Esters of cyclopropane acids that have either two carboxyl groups or a carboxyl and a ketonic group in combination with one of the ring carbon atoms are almost invariably transformed into open chained compounds by alcoholates, and not infrequently the same change is brought about by concentrated alkalies.[1] Esters of other cyclopropane acids rarely undergo this reaction, the one case known being that reported by Buchner and Miller.[2]



In connection with an investigation of the mechanism of this reaction it became desirable to examine the behavior of a cyclopropane derivative which is so constituted that it can form a metallic derivative without opening the ring. The substance selected for the purpose is benzoylphenyl nitrocyclopropane.



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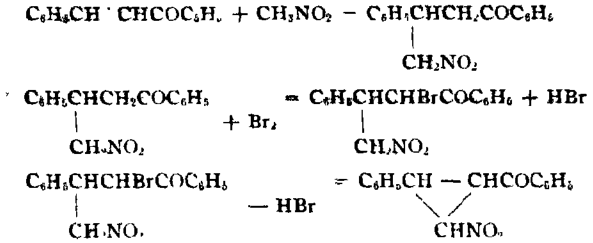
[1] *Ber.*, **36**, 3776 (1903); THIS JOURNAL, **39**, 1406, 1700, 2404 (1917).

[2] *Ber.*, **27**, 871 (1894).

Cyclopropane derivatives in which one of the ring carbon atoms holds a nitro group are unknown, but a feasible plan for preparing such substances was outlined in an earlier paper. This was adopted in the present work, with excellent results. It involves 3 reactions which are represented by the equations

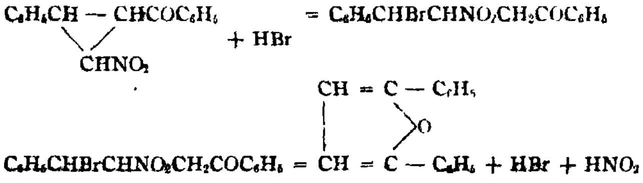


$$C_6H_5CH{:}CHCOC_6H_5 + CH_3NO_2 = C_6H_5\underset{\textstyle CH_2NO_2}{\underset{|}{C}H}CH_2COC_6H_5$$

$$C_6H_5\underset{\textstyle CH_2NO_2}{\underset{|}{C}H}CH_2COC_6H_5 + Br_2 = C_6H_5\underset{\textstyle CH_2NO_2}{\underset{|}{C}H}CHBrCOC_6H_5 + HBr$$

$$C_6H_5\underset{\textstyle CH_2NO_2}{\underset{|}{C}H}CHBrCOC_6H_5 - HBr = \begin{array}{c} C_6H_5CH - CHCOC_6H_5 \\ \diagdown\;\diagup \\ CHNO_2 \end{array}$$

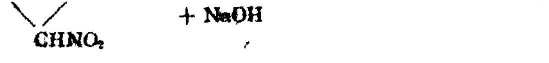
That the resulting nitro compound is a cyclopropane derivative and not an isomeric ethylenic ketone is shown not only by its indifference to permanganate but also by its behavior towards hydrogen bromide. In glacial acetic acid the substance combines with hydrogen bromide as readily as the most active α,β-unsaturated ketone, but the resulting compound is far more stable on heating than any saturated bromine compound which has bromine β to a carbonyl group. By eliminating both hydrobromic acid and nitrous acid it is possible to transform the addition product quantitively into 1,4-diphenyl furane. A compound having two phenyl groups in the 1,4-positions can be formed from one having them in the 1,3-positions only by closing a cyclopropane ring and opening it again at a different point. The reactions involved are therefore represented by the following equations:



$$\begin{array}{c} C_6H_5CH - CHCOC_6H_5 \\ \diagdown\;\diagup \\ CHNO_2 \end{array} + HBr = C_6H_5CHBrCHNO_2CH_2COC_6H_5$$

$$C_6H_5CHBrCHNO_2CH_2COC_6H_5 = \begin{array}{l} CH = C - C_6H_5 \\ |\qquad\quad \rangle O \\ CH = C - C_6H_5 \end{array} + HBr + HNO_2$$

The cyclopropane derivative is exceedingly sensitive to all alkaline reagents, the ring being opened even more easily than that of cyclopropane derivatives which have two carbonyl groups in combination with one of the ring carbon atoms. The process is accompanied by replacement of the nitro group and the final product is a β-diketone formed in accordance with the equation



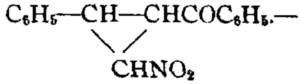
$$\begin{array}{c} C_6H_5CH - CHCOC_6H_5 \\ \diagdown\;\diagup \\ CHNO_2 \end{array} + NaOH = C_6H_5CH_2COCH_2COC_6H_5 + NaNO_2.$$

The reaction takes place in steps, but no intermediate products could be isolated. The discussion of the mechanism will therefore be deferred until the reaction has been studied with more favorable material.

Experimental Part.

The addition of nitro methane to benzal-acetophenone and the bromination of the product were carried out as described in an earlier paper.[1] The melting points of the isomeric α-bromo compounds are 100° and 106° instead of 100° and 86° as there given. The compound melting at 100°, the principal products can easily be transformed into the higher melting isomer by dissolving it in alcohol and saturating the solution with hydrogen bromide. The isomer separates slowly in almost quantitative yields. The transformation can also be effected by adding a small quantity of either toluidine or diethyl aniline to a methyl alcoholic solution of the lower melting isomer but the yield is much less and the product is contaminated with uncrystallizable red oils.

1-Benzoyl-2-phenyl-3-nitro Cyclopropane,



$$C_6H_5{-}\underset{\diagdown\ \diagup \atop CHNO_2}{CH{-}CH}COC_6H_5.{-}$$

The cyclopropane ring can be closed by eliminating hydrogen bromide from the bromine compound with a number of alkaline reagents, but the yields are unsatisfactory with all of them. The best results were obtained with potassium acetate, and the higher melting bromine compound gives a better yield than its isomer. When concentrated solutions of the low melting bromine compound are used, the higher melting isomer frequently crystallizes from the solution and then disappears again during the course of the reaction. Most of the material used in the investigation was made by starting with a thoroughly washed and dried mixture of the bromine compounds. The procedure was as follows:

A concentrated solution of 15 g. of fused potassium acetate in alcohol was added to a suspension of 15 g. of the mixed bromine compounds in 100 cc. of the same solvent. The mixture was allowed to remain at the ordinary temperature for an hour during which the bromine compounds dissolved and considerable quantities of potassium bromide and solid cyclopropane derivative separated. It was then heated on a steam bath for another hour to complete the reaction. The resulting solution, which was pale yellow when pure bromine compounds were used and brown if the materials were impure, was cooled in a freezing mixture and gradually diluted with water while being shaken vigorously. The cyclopropane derivative was precipitated as a crystalline, yellow solid which after one recrystallization from alcohol became colorless and melted at 98°. The yield varied from 55 to 75%—the average of a number of preparations being 61%. The filtrates contained yellow or brown uncrystallizable oils.

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[1] This Journal, 38, 889 (1916).

The cyclopropane derivative crystallizes in clusters of stout prisms. It is moderately soluble in alcohol and ether, readily in boiling alcohol, acetone and chloroform. When exposed to sunlight it gradually becomes tinged with pink.

Calc. for $C_{16}H_{13}O_3N$: C, 71.9; H, 4.9. Found: C, 71.6; H, 4.9.

Addition of Hydrogen Bromide.—Thirty g. of finely powdered cyclopropane derivative was added in small portions to 100 cc. of glacial acetit acid which had been saturated with hydrogen bromide. The substancc dissolved rapidly on shaking, the solution became warm, and the produce began to separate in crystalline form as soon as the solution started to cool. The mixture was allowed to stand for an hour during which most of the product separated, then poured into cracked ice. The colorless, pasty precipitate completely solidified when stirred. The solid was thoroughly washed with water, dried in the air and recrystallized from a mixture of acetone and ether.

Calc. for $C_{16}H_{14}O_3NBr$: C, 55.2; H, 4.0. Found: C, 55.5; H, 4.3.

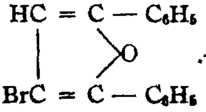
β-Nitro-γ,γ-bromo-phenyl Butyrophenone, $C_6H_5CHBrCHNO_2CH_2CO\cdot C_6H_5$, crystallizes in colorless plates which melt at 115–116° and decompose at 120°. It is an exceedingly sensitive substance. Unless perfectly pure it decomposes spontaneously at the ordinary temperature and in the dark. When the carefully purified compound is kept near the melting point for a short time or exposed to direct sunlight it turns yellow, and the color persists on recrystallization but the melting point remains constant at 115–116° and the composition remains the same.

Calc. for $C_{16}H_{14}O_3NBr$: C, 55.2; H, 4.0. Found: C, 55.3; H, 4.3.

When alcoholic solutions of the bromine compound are boiled they become acid. Qualitative experiments showed that the substance loses both hydrobromic and nitrous acids. The process is very slow but is greatly accelerated by addition of a small quantity of ammonium bromide. Thus 2 g. of ammonium bromide was added to a solution of 5 g. of the bromine compound in 40 cc. of methyl alcohol and the mixture boiled. In less than an hour all the substance had dissolved. The yellow solution, on cooling, deposited the product in pale yellow flakes, which after washing and recrystallization from alcohol melted at 90°.

Calc. for $C_{16}H_{12}O$: C, 87.3; H, 5.5. Found: C, 87.1; H, 5.1.

The substance has the composition of a diphenyl furane, and it was identified as 2,5-diphenyl furane by comparison with a specimen prepared according to Perkin.[1]

1,5-Diphenyl-3-bromo Furane,  .—When the hydrobromic acid addition product was heated above the melting point it lost oxides of nitrogen and water but no bromine or hydrobromic acid. The resulting greenish yellow melt was recrystallized from methyl alcohol. It consisted almost entirely of a pale yellow substance which crystallized in thin plates, resembling diphenyl furane, and melted at 77°. These were contaminated with a small quantity of a much yellower product which it was impossible to remove by recrystallization but which was finally got rid of by distillation under diminished pressure.

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[1] *J. Lond. Chem. Soc.*, 57, 954 (1890).

Calc. for $C_{16}H_{11}OBr$: C, 64.2; H, 3.7. Found: C, 64.6; H, 3.9.

The composition indicated loss of water and nitric oxide from the addition product. The substance is indifferent to permanganate but combines with two atoms of bromine when exposed to the action of bromine vapor. The bromine is completely unreactive—sodium methylate neither replaces it nor eliminates hydrogen bromide. The only open chained formula consistent with these properties is that of an allenic ketone.

$$C_6H_5CHBrCHNO_2CH_2COC_6H_5 = C_6H_5CBr = C = CHCOC_6H_5 + H_2O + NO.$$

We could not, however, secure any evidence of the presence of a carbonyl group, as it was impossible to make either a hydrazone of an oxime. In view of its great stability it seems more probable, therefore, that it is a furane derivative as written. The formation of a furane derivative involves a shifting of the bromine atom, but similar shifts have been observed before in high temperature reactions involving ring formation.

Action of Bases on the Cyclopropane Derivative.—The cyclopropane derivative is readily attacked by all bases but it is difficult to get definite products from the resulting brown or red oils. The following procedure, however, proved fairly satisfactory: An excess of concentrated sodium methylate was added gradually to a well cooled solution of 10 g. of cyclopropane derivative in the minimum quantity of methyl alcohol. The mixture was left at the ordinary temperature for 8 hours, then acidified with hydrochloric acid, and allowed to evaporate in the air. The resulting yellow oil was dissolved in ether and this solution shaken with a saturated aqueous solution of copper acetate. This gave 7 g. of a pale copper derivative. The copper derivative, after decomposition with sulfuric acid in the usual way, yielded a colorless solid which crystallized in plates and melted at 54°.

Calc. for $C_{16}H_{14}O_2$; C, 80.7; H, 5.9. Found: C, 80.6; H, 6.1.

The composition and melting point of the substance as well as the melting point of its copper derivative indicated phenyl-acetyl-acetophenone.

This diketone was therefore made by condensing ethyl phenylacetate with acetophenone. A mixed melting point showed that the two products are identical.

The diketone is not the primary product of the reaction between bases and the cyclopropane derivative. If the alcoholic solution containing the product of the reaction with sodium methylate is acidified with acetic instead of hydrochloric acid, and then allowed to evaporate it leaves an oil that contains no nitrogen but gives only a trace of copper derivative. When this oil is digested for a short time with a dilute solution of hydrochloric acid in methyl alcohol, and then shaken with copper acetate it gives the usual amount of copper derivative, showing that the oil contains an intermediate product which is turned into diketone by the action of mineral acids. All efforts either to isolate this product or to acquire more information about it were unsuccessful.

CAMBRIDGE, MASS

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, KENTUCKY AGRICULTURAL EXPERIMENT STATION]

THE COMPOSITION OF THE ASH OF CRAB GRASS (DIGITARIA SANGUINALIS) AS AFFECTED BY THE SOIL IN WHICH IT IS GROWN.

BY G DAVIS BUCKNER

Received June 4, 1919.

Plant nutrition teaches that the chemical composition of the ash of the same species of plant varies within wide limits when grown in different localities and under different conditions. Plants flourish when grown in soils of widely varying composition and seem to require no definite medium from which to secure the nourishment necessary for normal growth, provided it does not fall below a certain quantitative and qualitative level. The ash of plants grown in different soils will likewise have a variable composition.

In the prosecution of certain experiments in this laboratory it was found desirable to obtain a green plant which contained a large percentage of ash, the composition of which would satisfy given conditions. In the search for such a plant it was noticed that crab grass (*Digitaria sanguinalis*) grew and flourished in the middle of a limestone roadway. From other experiments it was reasoned that here at least would be conditions most favorable for the largest intake of calcium. The comparative analysis of a plant grown under such conditions and that of a sample of the same species grown under normal condition of garden soil would have an added interest. For these reasons plants were carefully selected with regard to form and size, and cut one inch above the ground, and from all external appearances they were similar. Both samples were immediately washed with distilled water to free them from extraneous material and were analyzed for calcium, magnesium, phosphorus, silicon and potassium. The results are shown in the following table.

Table I.—Analyses of Crab Grass Ash.

	Grown in garden soil G	Grown in limestone roadway G	Percentage difference
Wt. of air-dried sample	7 9833	7 8307	
Wt of ash of air-dried sample	1 6640	1 3695	
	%	%	
Ash in the air-dried sample	20 84	17 49	—16 1
P_2O_5 in the ash	4 01	4 92	+22 7
SiO_2	14 60	14 50	
CaO	3 75	5 40	+44 0
MgO	2 68	3 42	+27 6
K_2O	39 86	32 38	—18 8

It will be seen from these figures that the intake of inorganic material was not the same in the two specimens. It is interesting to note that the sample of grass grown in the middle of a comparatively new limestone roadbed which was from 4 to 5 inches in thickness contained approximately 16% less ash than did a similar sample grown in garden soil and that the quantity of K_2O was 18.8% less in the first mentioned. In opposition to this it is seen that the ash of the sample grown in the limestone contained 22.7% more P_2O_5, 44 0% more CaO and 27 6% more MgO. That the percentage of silica is approximately the same in these two samples is likewise worthy of note.

The outstanding feature in connection with the growth of these two samples of crab grass is that the absorption and retention of these different amounts of calcium, magnesium, phosphorus and potassium cause no observable difference in their external appearance.

Lexington, Ky

[Contribution from the Chemical Laboratory of the Ohio State University.]

THE OXIDATION OF ORGANIC COMPOUNDS WITH ALKALINE POTASSIUM PERMANGANATE.

Part I.—The Oxidation of Acetaldehyde. Part II.—The Oxidation of Glycol, Glycollic Aldehyde, Glyoxal, Glycollic Acid and Glyoxalic Acid.

By William Lloyd Evans and Homer Adkins.

Received June 20, 1919

The problem of the alkaline oxidation with potassium permanganate of some of the simple alcohols, aldehydes, ethers, ketones and acids has been quantitatively studied by a number of investigators.[1] In much of the work which has been done on the alkaline oxidation of organic compounds no systematic study has been made of the effect of the added alkali on the nature of the reaction products. The work reported in this paper is a continuation of the experiments begun by Day and one of us on the oxidation of ethyl alcohol. This paper deals with the following phases of the problem:

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[1] Nef, *Ann.*, 335, 269 (1904); Denis, *Am. Chem. J.*, 38, 561 (1907); Evans and Witzemann, This Journal, 34, 1086 (1912); Witzemann, *Ibid.*, 38, 150 (1916); 39, 2657 (1917); Evans and Day, *Ibid.*, 38, 375 (1916); Evans and Day, *Ibid.*, 41, 1267 (1919).

PART I.—The oxidation of acetaldehyde with potassium permanganate in neutral solutions and in those containing from 200 to 400 g. of potassium hydroxide per liter has been carried out at temperatures of 25, 50 and 75°. The products of oxidation have been determined quantitatively.

PART II.—The oxidation of glycol, glycollic aldehyde, glyoxal, glycollic acid and glyoxalic acid at a temperature of 50° and at various concentrations of potassium hydroxide has been made, and the amounts of oxalic acid and carbon dioxide produced determined.

The data obtained is discussed from three standpoints:

1. The relationship of potassium hydroxide concentration to the products of oxidation.

2. The relationship of temperature to the products of oxidation.

3. Deductions as to the relationship of the compounds during alkaline oxidation.

PART I.—THE OXIDATION OF ACETALDEHYDE.

Historical Discussion.

A search of the literature revealed the fact that very little work has been done in studying the oxidation of this compound. The three more important reports are as follows:

Heimrod and Levene[1] oxidized acetaldehyde in an alkaline solution with hydrogen peroxide. They studied the possible intermediate oxidation products: glycollaldehyde; glyoxal; glycollic and glyoxylic acid, estimating in each case the amounts of carbon dioxide and formic acid formed. They give equations showing the various possible courses of the oxidation. They conclude that acetaldehyde oxidizes through the following stages: acetaldehyde ⟶ (vinyl alcohol) ⟶ glycol aldehyde ⟶ glyoxal ⟶ formic acid ⟶ carbon dioxide. They claim that there is no evidence of the formation of formaldehyde as an intermediate product.

In view of the fact that acetaldehyde is a good depolarizer, Law[2] oxidized it electrolytically and obtained carbon monoxide and dioxide as well as acetic acid. Formic acid was formed in small amounts. In 0.85 *N* sulfuric acid acetaldehyde was oxidized almost quantitatively to acetic acid.

Denis[3] conducted two experiments, one in an 8.5 molar alkaline solution, and one in a neutral solution. In the alkaline solution a 75% yield

[1] *Biochem. Z.*, 29, 31–39 (1910).

[2] *Trans. Chem. Soc.*, 87, 198 (1905).

[3] *Am. Chem. J.*, 38, 569 (1907).

of acetic acid was obtained together with oxalic acid and carbon dioxide. In the neutral solution after oxidation of the aldehyde only acetic acid was found (96.8% yield). The absence of formic acid was proven.

Experimental Part.

1. **The Preparation of the Aldehyde Solution.**—Acetaldehyde was prepared by the method described by McLeod.[1] Paraldehyde was depolymerized by the use of dil. sulfuric acid (1 · 4). The product of the first distillation after treatment with the acid, was redistilled twice, the fractions coming over below 27° being used in making the standard aldehyde solution. The final distillate contained probably 1–2% of water as shown by the slight coloring of dehydrated copper sulfate. A weighed amount of the aldehyde so prepared was dissolved in water in such a proportion that a two molar solution was obtained.

2. **The Standard Potassium Hydroxide Solution.**—A concentrated potassium hydroxide solution was made and standardized by titrating with 0.5 *N* sulfuric acid. The solution contained 0.445 g. of potassium hydroxide per cc. The carbon dioxide content was ascertained to be 0.0027 g. per cc.

3. **The Oxidation.**—The oxidations were carried on in two-liter balloon flasks. The flasks were supplied with rubber stoppers through which extended a piece of glass tubing, a pipet, and a stirring rod placed in a mercury seal. The stirring rod was attached to a revolving spindle by means of rubber tubing, the glass tubing by the same means to a buret. The oxidizing solution was prepared as follows· A measured amount of the concentrated potassium hydroxide solution was made up to a volume of one liter by the addition of carbon dioxide-free water. Fifteen g. of potassium permanganate were then placed in the alkaline solution.

The flask was placed in the electrically controlled thermostat, and then the motor stirring device and the buret containing the aldehyde solution were attached. When the permanganate had dissolved and the solution had reached the temperature of the thermostat the acetaldehyde was added very slowly until complete decolorization of the permanganate had been accomplished. This point could be determined by drawing the mixture up into the pipet and allowing the precipitated manganese dioxide to settle. The change was from pink to colorless in the neutral and weak alkali (0 to 9 g. of potassium hydroxide per liter) and from green to colorless in the stronger alkali solutions.[2] At 25° on account of the slowness of oxidation it was necessary to allow the mixture to stand several hours between every two additions of 0.1 cc. of the aldehyde solutions when the end-point was almost reached. At 50° the portions added were completely oxidized within less than an hour, even in the case of weak alkali solutions. That the end-point could be ascertained with a fair degree of accuracy is shown by the fact that oxidations carried on two months apart checked with each other within less than 8 mg. of acetaldehyde oxidized, that is, within one drop of the standard solution.

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[1] *Am. Chem. J.*, **37**, 27 (1907).

[2] Compare Evans and Day, THIS JOURNAL, **41**, 1271 (1919).

The reaction mixture was filtered in a specially constructed carbon dioxide-free apparatus designed by Evans and Day[1] and the filtrate was made up to a volume of two liters and analyzed.

An aliquot part of this solution was acidified (using a drop on phenolphthalein solution as an indicator) with acetic acid, then ammonium hydroxide added until the reaction was alkaline. The oxalic acid was then precipitated from the hot solution by the use of a 5% solution of calcium acetate. After filtering and washing, the precipitate was dissolved in 15 cc. of sulfuric acid (1:4). 130 cc. of distilled water was added and the hot solution was then titrated with 0.098 *N* potassium permanganate solution.

The carbon dioxide was determined by means of the Foulk apparatus,[2] the carbon dioxide being absorbed in Liebig bulbs, proper correction being made for the carbon dioxide in the standard potassium hydroxide.

The acetic acid was determined by the method of Stillwell and Gladding. *Much difficulty has been experienced in the determination of this* acid by various analysts. The following procedure when precisely followed gives excellent results, as evidenced by the fact that in 25 determinations of acetic acid it was unnecessary to repeat a single one, two samples from the same solution never varying from each other to a greater extent than 0.2 cc. of 0.1 *N* sodium hydroxide solution and in most cases the determinations were in agreement to within 0.05 cc. Experiments showed that the recovery of acetic acid was 99.8 to 100%.

The apparatus for this determination of acetic acid consisted of a 500 cc. balloon flask fitted with a two-hole stopper through which extended the stem of a dropping funnel, and a Kjeldahl bulb. The Kjeldahl bulb was connected to a Leibig condenser which in turn ended in a cylindrical dropping funnel which was graduated into 25 cc. divisions. The dropping funnel was connected by a two-hole stopper to a 750 cc. Erlenmeyer flask.

The sample (100 cc.) was put into the balloon flask together with bits of porous plate, the flask stoppered and 20 cc. of syrupy phosphoric acid added. Distillation was then begun. When 50 cc. of distillate had collected in the dropping funnel, 25 cc. of hot water was then added and the operations continued, thus maintaining the volume in the distilling flask between 70 and 95 cc. When the distillate had reached a volume of 400 cc. it was found that in all cases the acetic acid had been completely distilled over. In case the alkali present in the sample exceeds 3 g. it is necessary to add considerably more than the 20 cc. of phosphoric acid plus the amount required to neutralize the excess of alkali. If the amount of alkali is as much as 12 g. it is advisable to use 40 cc. of phosphoric acid. If this precaution is not taken the final portions of the acetic acid distil over very slowly. The use of fresh pieces of porous plate shortens the time of distillation about 45 minutes. It reduces the necessary volume of the distillate about 100 cc. and especially with samples high in alkali it is very valuable in preventing the otherwise almost inevitable bumping. The distillate was freed of carbon dioxide by bubbling carbon dioxide-free air through it for 10 minutes, after which it was titrated with 0.1 *N* alkali using phenolphthalein as an indicator. Preliminary experiments showed that results were from one to 3% too high if the precaution was not taken of removing the carbon dioxide.

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[1] *Loc. cit.*

[2] Foulk's "Notes on Quantitative Analysis," 1914, p. 222. McGraw-Hill Book Co.

Explanation of Data Sheet and Curves.

1. Method of Tabulating Results.—All of the 20 oxidations here reported were checked at least once and in several cases checked 3 or more times. The analytical data are the result of at least two analyses of the same solution. The liberty has been taken of discarding a few experiments, the results of which were quite obviously in error due to faulty manipulation, or variation in temperature of the bath during the process of oxidation.

The weight of potassium hydroxide placed in the oxidizing flask is given the first column, the larger figure in parenthesis is the volume in cc. of the solution at the end of the oxidation. The weights of acetic and oxalic acids and carbon dioxide which were found in the solution upon analysis are given Cols. 2, 3 and 4. The aldehyde equivalent of these products is given Col. 5. The weights of acetic and oxalic acid and carbon dioxide which would be produced if 4.4 g. (0.1 mol. wt.) of acetaldehyde were oxidized under the conditions of the experiment are given in Cols. 6, 7 and 8. The figures in Col. 9 give in g. the amount of oxalic acid which would be produced if 4.4 g. of the acetaldehyde equivalent of some intermediate compound were oxidized to oxalic acid and carbon dioxide in the ratio in which they are produced at the given concentration of potassium hydroxide; for example, if in a given experiment one g. of oxalic acid and one g. of carbon dioxide were produced, the acetaldehyde equivalent would be 0.49 and 0.5 g., respectively, or a total of 0.99 g. acetaldehyde. Thus if 0.99 g. of acetaldehyde gave one g. of oxalic acid, then 4.4 g. of acetaldehyde would give 4.44 g. of oxalic acid. Similar values for carbon dioxide production are given in Col. 12. The figures in Col. 10 give in grams the average concentration of potassium hydroxide during the oxidation. Col. 11 contains the weights of aldehyde which were added to reduce the permanganate solution. These

TABLE I

The Oxidation of Acetaldehyde at Various Temperatures and Concentrations of Potassium Hydroxide.

G KOK.	CH_3COOH	$(COOH)_2$	CO_2	G CH_3CHO recovered as oxidation products	$\frac{CH_3COOH}{4.4 \text{ gr } CH_3CHO}$	$\frac{(COOH)_2}{4.4 \text{ gr } CH_3CHO}$	$\frac{CO_2}{4.4 \text{ gr } CH_3CHO}$	$\frac{4.4\,(COOH)_2}{\frac{CO_2}{0.50}+\frac{(COOH)_2}{0.49}}$	KOH Av g per L	CH_3CHO added	$\frac{4.4\,CO_2}{\frac{CO_2}{0.50}+\frac{(COOH)_2}{0.49}}$.
1	2	3	4	5	6	7	8	9	10	11	12
					Oxidation at 25°						
4.45 (1058)	6.17	0.306	0.46	4.89	5.53	0.275	0.414	3.57	3.60	5.00	5.31
8.9 (1049)	4.82	0.62	0.68	4.16	5.09	0.655	0.70	4.18	8.25	4.22	4.72
13.35 (1043)	3.92	0.70	0.70	3.565	4.84	0.87	0.87	4.43	13.0	3.74	4.47
44.45 (1036)	2.95	1.128	0.76	3.07	4.20	1.61	1.09	5.31	43.65	3.13	3.61
175	2.46	1.37	0.68	2.814	3.84	2.14	1.06		173.0	2.89	
200	2.50	1.38	0.70	2.86	3.85	2.13	1.08		197.0	2.92	
					Oxidation at 50°						
4.45 (1037)	3.32	0.67	0.90	3.22	4.52	0.915	1.23	3.80	4.5	3.26	5.09
8.9 (1033)	2.41	0.925	0.98	2.71	3.91	1.51	1.60	4.30	9.05	2.77	4.57

13.35 (1028)	1.90	1.02	0.94	2.34	3.56	1.92	1.77	4.63	13.7	2.42	4.28
22.25 (1025)	1.58	1.18	0.90	2.19	3.18	2.37	1.82	5.06	22.6	2.26	3.86
44.5 (1025)	1.42	1.306	0.90	2.13	2.93	2.69	1.85	....	44.4	2.20	....
89 (1025)	1.44	1.33	0.91	2.16	2.91	2.70	1.85	....	88.7	2.20	....
					Oxidation at 75°.						
4.45 (1028)	1.90	0.95	1.24	2.49	3.37	1.68	2.19	3.86	4.7	2.53	5.02
8.9 (1025)	1.266	1.225	1.185	2.113	2.64	2.55	2.45	4.49	9.3	2.16	4.41
13.35 (1023)	1.05	1.35	1.15	2.00	2.31	2.97	2.53	4.82	13.8	2.04	4.09
44.45 (1022)	0.90	1.353	1.12	1.89	2.09	3.15	2.60	....	44.5	1.94	....
89.0 (1022)	0.91	1.36	1.14	1.91	2.09	3.14	2.62	....	88.8	1.95	....
					"Neutral Solution" at Various Temperatures.						
....	7.93	...	...	5.82	6.0	....	....	....	acid	5.94	....
....	7.98	...	...	5.96	6.0	....	....	....	acid	5.96	....
....	7.91	...	...	5.80	6.0	....	....	....	acid	5.91	....

weights are based on the weights of the prepared aldehyde used in making the reducing solution.

That the substance weighed out as aldehyde was not free from water is shown by the slight coloring of dehydrated copper sulfate noted above and by the fact that there is a constancy of yield of 97–98% when the yield is calculated on the basis of the weighed substance being free from water. The work of Denis[1] showed that acetaldehyde as prepared by McLeod[2] was about 97% pure.

2. **To Determine the Concentration of Alkali.**—At the beginning of the oxidation, the alkali concentration is known through the method for the preparation of the oxidizing mixture. However, as soon as oxidation begins, other factors determine the concentration at any given time. The three factors which are taken into consideration in calculating the "average potassium hydroxide" given in Col. 10 of the table are as follows· (*a*) The 15 g. of potassium hydroxide according to the equation $2KMnO_4 + H_2O = 2KOH + 2MnO_2 + 3O$, this results in an increase in the amount of potassium hydroxide in the oxidizing solution. (*b*) The acetic, oxalic and carbonic acids produced by oxidation will neutralize a certain amount of the potassium hydroxide. (*c*) As the aldehyde solution is added the volume of the alkali solution is increased and consequently the concentration of the alkali is decreased.

Thus, through factor (*a*) the concentration of alkali is increased and through factors (*b*) and (*c*) it is decreased. In plotting the curves the alkali ordinate is found as follows The amount of hydroxide necessary to give potassium oxalate, potassium hydrogen carbonate and potassium acetate is found. This amount taken from the total amount of potassium hydroxide introduced (*i. e.*, the weight originally put in plus 5.3 g.) gives the number of grams of potassium hydroxide present at the end of the oxidation. This amount divided by the volume of the solution in cc. and the quotient multiplied by 1000 gives the concentration per liter of alkali at the end of the oxidation. The mean between this concentration and the concentration at the beginning of the oxidation is taken as the average concentration during the course of the experiment. Under some conditions the factors almost balance each other, while in others (first expt. at 25° for example) the correction is about 0.85 of a g. of potassium hydroxide, almost $^1/_6$ of the amount of potassium hydroxide originally added. In any event, these corrections can only be approximate.

Another factor which has not been considered in the calculations which probably does effect the alkali concentration is that the precipitated manganese compound or compounds holds some potassium in chemical union. Morawski and Stingl,[1] and Smolka[2] and Gmehlin-Kraut-Friedman[3] point out that the compound KH$_3$Mn$_4$O$_{10}$ is formed. There is uncertainty as to the exact composition of this substance. Furthermore, there is no data as to the effect of the alkali concentration upon its formation. For these reasons the potassium which may be withdrawn from the solution due to the formation of this compound is not considered in the calculations.

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[1] *Am. Chem. J.*, 38, 567 (1907).

[2] *Ibid.*, 37, 27 (1907).

3. **Plotting the Graphs.**—In Fig. 1 the weights of acetic acid which would be produced by 4.4 g. acetaldehyde at the given concentration of alkali are plotted against the grams of potassium hydroxide per liter, present during the oxidation. In Figs. 2 and 3 the weights of oxalic and carbon dioxide are so plotted. In Fig. 4 the acetic acid-alkali relationship is plotted on logarithmic paper.

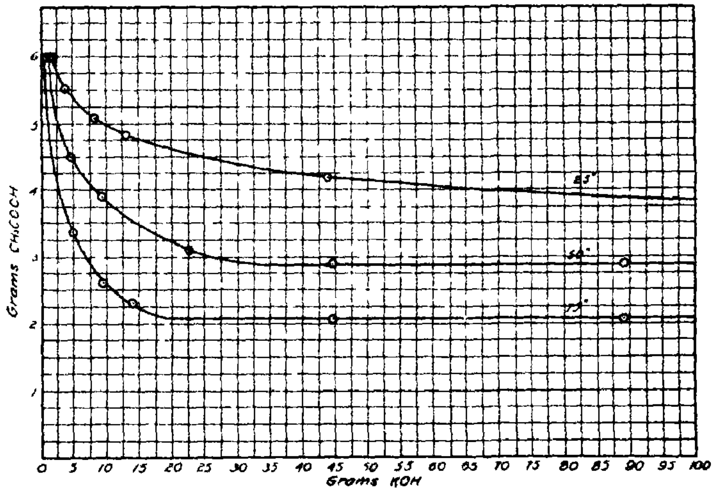

Fig. 1.—Acetic acid produced by 4.4 g acetaldehyde

The weight of oxalic acid (Col. 9 of Table I) which would be produced if 4.4 g. of acetaldehyde (or its equivalent) were oxidized to oxalic acid and carbon dioxide in the ratio in which they are produced in the given experiment is plotted against potassium hydroxide concentration in Fig. 5.

Three results (Table I) are given of oxidations carried out in "neutral solution," that is, no potassium hydroxide was added to the oxidizing solution. Since the potassium hydroxide produced by hydrolysis was insufficient to neutralize the acetic acid produced by oxidation, the oxidation in reality took place in a weakly acid solution. These oxidations took place at different temperatures from 25 to 75°. It is necessary to filter and analyze these solutions immediately, for the weakly acid solution is

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[1] *J. prakt. Chem.*, [2] 18, 86 (1878); *Jahresb.*, 5, 275 (1878).

[2] *Sitzungber. Math. Naturwissensch. Klasse Kais Akad. Wissensch. Wein*, 95, II, 5-30 (1887).

[3] *Handb. Anorg. Chem.*, 3, II, 254.

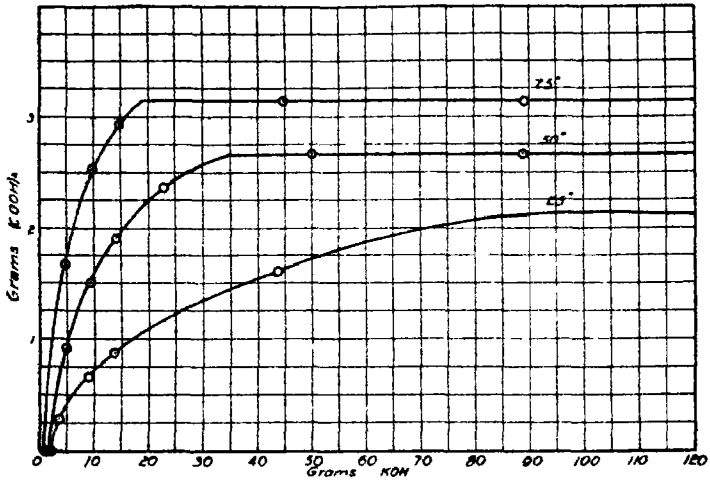

Fig. 2.—Oxalic acid produced by 4.4 g. acetaldehyde.

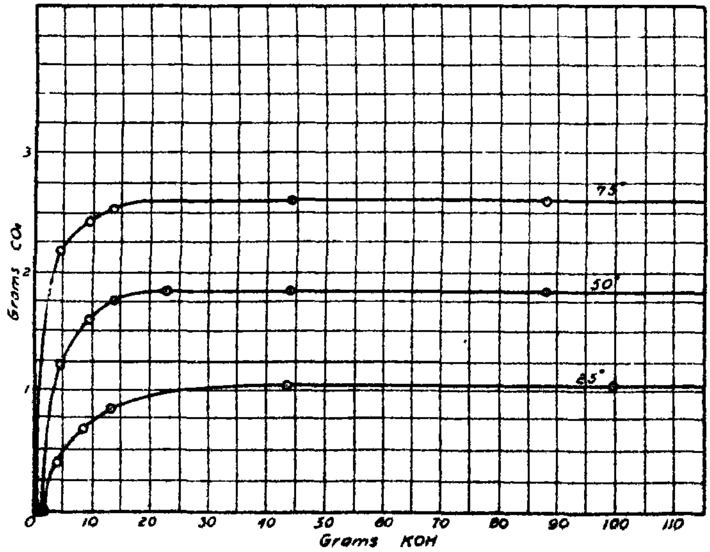

Fig. 3.—Carbon dioxide produced by 4.4 g. acetaldehyde.

apparently an ideal media for the growth of certain organisms. Large masses of these develop in a few days.

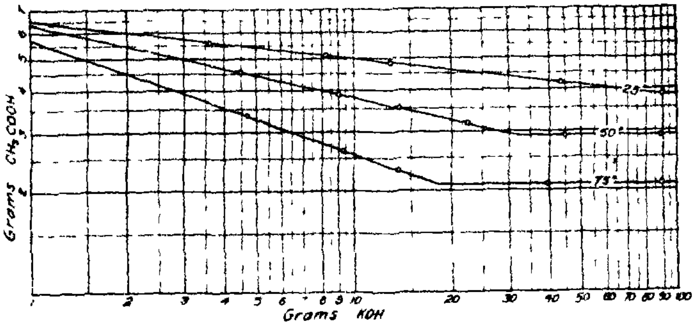

Fig 4.—Acetic acid alkali relationship

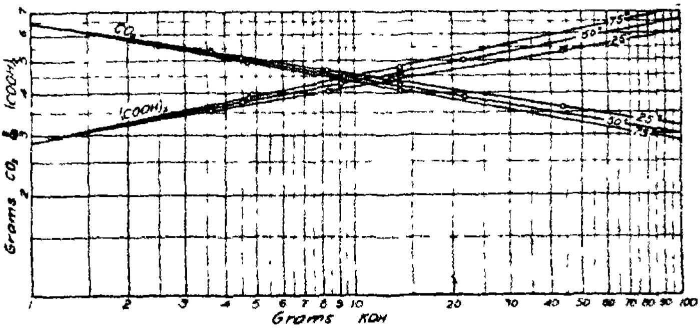

Fig. 5 —Oxalic acid and carbon dioxide produced by 4.4 g acetaldehyde.

Discussion.

Acetic Acid.—The formation of acetic acid from acetaldehyde is to be expected. The mathematical relationship of the amounts of acetic acid produced to the average alkali concentration may be derived as follows: The fact that the acetic acid-alkali concentration relation gives a straight line when plotted on logarithmic paper means that the relation connecting these two quantities is expressed by the following equation:

$$Y = \frac{B}{X^a}$$

where Y equals the number of g. of acetic acid produced by the oxidation of 0.1 M g. of acetaldehyde at a concentration of X g. of potassium hydroxide per liter, and a is the tangent of the angle which the line makes with the X axis. This equation may be written as follows:

$$\log Y = \log B - a \log X$$

When $X = 1$, the second term on the right side of the equation disappears. The value of B is then found to be equal to the ordinate when the abscissa is one. The values for B and a at the temperatures employed in these experiments are shown in the following equations:

$$Y = 6.49\, X^{-0.114} \text{ at } 25^\circ \tag{1}$$

$$Y = 6.38\, X^{-0.226} \text{ at } 50^\circ \tag{2}$$

$$Y = 5.70\, X^{-0.342} \text{ at } 75^\circ \tag{3}$$

It is of much interest in this connection to note that the above equation is the same one found for the amount of acetic acid formed when ethyl alcohol is oxidized with alkaline potassium permanganate.[1]

It will be observed that the value of the tangent of the angle decreases about 0.114 for each lowering of 25° in the temperature. This indicates that at about 0° the tangent of the angle would be zero, or in other words, at that temperature the line would be parallel to the X axis. That is, at 0° acetaldehyde would be oxidized quantitatively to acetic acid no matter what was the alkalinity of the oxidizing solution. (See Fig. 13.) The weight of acetic acid which would be produced by the oxidation of 4.4 g. of acetaldehyde would be 6 g.

From a study of the logarithmic graph (Fig. 4), it will be seen that the acetic acid-potassium hydroxide line reaches the ordinate 6 at = 1.95, 1.3 and 0.85 for 25°, 50° and 75°, respectively, *i. e.*, those concentrations are the highest concentrations at those temperatures at which acetaldehyde is oxidized quantitatively to acetic acid. Or, stated in terms of Nef's dissociation theory, those are the concentrations of alkali at which the acetaldehyde begins to dissociate with the production of vinyl alcohol. These values are in accord with McLeod's statement noted below. As he does not report the temperature, an exact comparison is impossible.

The minimum amounts of acetic acid obtained are 3.84, 2.91, 2.09 at 25°, 50° and 75°, respectively. By reference to the logarithmic lines it will be seen that these values for the ordinate correspond to 90, 32.5 and 18.5 g., respectively. That is at those concentrations of potassium hydroxide per liter the minimum amount of acetic acid for those temperatures would be produced. Hence, the logarithm of the amount of acetic acid produced by the alkaline permanganate oxidation of acetaldehyde is a linear function of the logarithm of the potassium hydroxide concentration employed between the following limits: 1.95 g. to 90 g. at 25°; 1.3 to 3.25 g. at 50°; and 0.85 g. to 18.5 g. at 75°. At concentrations above the larger value, increase in potassium hydroxide affects no change in the amount of acetic acid, and at concentrations less than the smaller number the oxidation of acetaldehyde to acetic acid is quantitative. Hence, the equations derived, give correct values for Y only between certain limiting values of X.

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[1] Cf. Evans and Day, THIS JOURNAL, 41, 1282 (1911).

Oxalic Acid and Carbon Dioxide.—Evans and Day[1] in their paper on ethyl alcohol have shown that there is no good evidence for believing that oxalic acid is produced by the alkaline oxidation of acetates or that carbon dioxide is produced by the alkaline oxidation of oxalates or acétates.

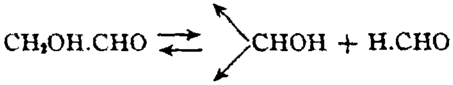
Denis[2] held that the formation of an olefin derivative (in this case vinyl alcohol) was *conditio sine qua non* of the oxidation of acetaldehyde to compounds other than the corresponding fatty acid. McLeod[3] showed that vinyl alcohol molecules did exist in an aqueous solution as soon as sodium hydroxide was present to the extent of 0.1%. The oxidation would then go through the following states:

$$CH_3 = CHO \text{ (in alkaline solution)} \rightleftarrows CH_2 = CHOH \qquad (1)$$

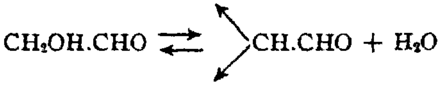
$$CH_2 = CHOH + 2OH \longrightarrow CH_2OH.CH(OH)_2 \qquad (2)$$

That glycollic aldehyde is one of the intermediate compounds in the oxidation of acetaldehyde is convincingly shown in Part II of this paper

Nef[4] postulated that glycollic aldehyde could dissociate as follows:



$$CH_2OH.CHO \rightleftarrows \, >CHOH + H.CHO \qquad (3)$$



$$CH_2OH.CHO \rightleftarrows \, >CH.CHO + H_2O \qquad (4)$$

The oxidation of the reaction products in (3) would yield carbon dioxide. If the reaction product in (4) is oxidized to glyoxal, then glycollic acid would be one of our intermediate compounds in these reactions since glyoxal and diketo compounds of the same type undergo simultaneous oxidation and reduction, *i. e.*, the benzilic acid rearrangement. It is shown in Part II that glycollic acid is ultimately oxidized to oxalic acid and carbon dioxide.

The alkali concentration might then be supposed to affect the production of vinyl alcohol molecules (cf. Part II). It also undoubtedly affects the reactions whereby oxalic acid and carbon dioxide are produced from the intermediate compounds, since it is evident from a study of the curves that the production of oxalic acid and carbon dioxide is affected by the variation in the concentration of the alkali.

It is important to consider the oxalic acid-alkali concentration relationship as given in Col. 9, Table I, and as plotted in Fig. 5. It is seen that this relationship as expressed on logarithmic paper is also a straight line. As noted above, the acetic acid-alkali concentration relationship plotted on logarithmic paper gives a straight line, showing that the logarithms of the amounts of acetic acid produced from acetaldehyde by the alkaline oxidation with potassium permanganate is also a linear function of the logarithm of the potassium hydroxide concentration. The fact that the relative production of oxalic acid and carbon dioxide may be expressed in a mathematical expression of the same type indicates that the alkali acts in the same general way upon the compound which is the source of these acids as it does upon the acetaldehyde which is a source of the acetic acid.

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[1] *Loc. cit.*

[2] *Am. Chem. J.*, 38, 368 (1907).

[3] *Ibid.*, 37, 23 (1907); cf. Nef, *Ann.*, 298, 316 (1897).

[4] *Ibid.*, 335, 274, 282 (1904).

The equations expressing the oxalic acid-alkali concentration and the carbon dioxide-alkali concentration involved in the oxidation of the acetaldehyde equivalent of the intermediate compound may be derived in the same manner as were those for the acetic acid-alkali concentration. If we let Z_o = grams of oxalic acid so produced; Z_c the grams of carbon dioxide; and X the grams of potassium hydroxide per liter, then the equations will be as follows:

For 25° $Z_o = 2.87\,X^{0.167}$ (4) $Z_c = 6.5\,X^{-0.155}$ (7)
For 50° $Z_o = 2.87\,X^{0.184}$ (5) $Z_c = 6.5\,X^{-0.166}$ (8)
For 75° $Z_o = 2.88\,X^{0.200}$ (6) $Z_c = 6.5\,X^{-0.176}$ (9)

If the amount of acetic acid produced (Equations 1, 2 and 3) is multiplied by the factor 0.733, the product will be the weight in grams of the acetaldehyde equivalent to the actic acid produced. It is evident that if this product is subtracted from 4.4 g. (the total amount of the aldehyde), the remainder will be the acetaldehyde equivalent (W) of the intermediate compound formed in these reactions which is oxidized to oxalic acid and carbon dioxide.

These amounts are found to be as follows:

For 25° $[4.4 - (0.733)(6.49\,X^{-0.114})]$ (10)
For 50° $[4.4 - (0.733)(6.38\,X^{-0.226})]$ (11)
For 75° $[4.4 - (0.733)(5.70\,X^{-0.342})]$ (12)

Equations 4 to 9 inclusive were calculated on the basis that 4.4 g. of acetaldehyde was oxidized to oxalic acid and carbon dioxide in the same ratio as that in which these two compounds were found as reaction products at the concentration of the alkali used. The actual amount of the intermediate compound which is the source of the oxalic acid and carbon dioxide in these reactions is not constant in amount for the same temperature but it depends upon the concentration of the alkali used. Furthermore, the ratio of the oxalic acid and carbon dioxide production from the oxidation of the intermediate compounds is also dependent upon the concentration of the alkali used. The aldehyde equivalent of the intermediate compounds is easily obtained by solving the equations in the preceding paragraph.

Thus we have at hand the data necessary for calculating the oxalic acid and carbon dioxide produced in the oxidation of acetaldehyde as well as the acetic acid production as noted above. For it Y_o = g. of oxalic acid produced by the oxidation of 4.4 g. of acetaldehyde at a concentration of X g. of potassium hydroxide per liter, then Y_o will bear the same relationship to the actual amount of the intermediate compound oxidized to oxalic acid and carbon dioxide as the values of Z_o (Equations 4 to 6 inclusive) bear to 4.4, *i. e.*,

$$Y_o : 4.4 - (0.733)(6.49\ X^{-0.114})] = 2.87\ X^{0.167} : 4.4. \qquad (13)$$

By solving the easily formed equations of this type the oxalic acid production from aldehyde can be readily calculated for any concentration of the alkali at the temperature represented by the equation. The following are the values of Y_o and Y_c (carbon dioxide production):

$$\text{At } 25^\circ\ Y_o = 2.87\ X^{0.167} - 2.090\ X^{0.063} \qquad (14)$$

$$Y_c = 6.5\ X^{-0.156} - 7.03\ X^{-0.269} \qquad (15)$$

$$\text{At } 50^\circ\ Y_o = 2.87\ X^{0.184} - 3.03\ X^{-0.042} \qquad (16)$$

$$Y_c = 6.5\ X^{-0.165} - 6.91\ X^{-0.291} \qquad (17)$$

$$\text{At } 75^\circ\ Y_o = 2.88\ X^{0.200} - 2.724\ X^{-0.510} \qquad (18)$$

$$Y_c = 6.5\ X^{-0.178} - 6.17\ X^{-0.518} \qquad (19)$$

The correlation of the values determined by experiment with the values found by solving the equations is shown in the following table:

TABLE II.—COMPARISON OF VALUES FOUND AND CALCULATED.

Temperature	Value of X	CH_3COOH Experiment	CH_3COOH Equation	$(COOH)_2$. Experiment.	$(COOH)_2$. Equation.	CO_2 Experiment.	CO_2 Equation
25°	3.6	5.53	5.57	0.275	0.255	0.41	0.39
25°	8.25	5.09	5.08	0.655	0.63	0.70	0.70
25°	13.0	4.84	4.83	0.87	0.87	0.87	0.89
25°	43.65	4.20	4.24	1.61	1.62	1.09	1.08
50°	4.5	4.52	4.54	0.92	0.93	1.23	1.23
50°	9.05	3.91	3.89	1.51	1.53	1.60	1.60
50°	13.7	3.56	3.56	1.92	1.92	1.77	1.74
50°	22.6	3.18	3.18	2.37	2.42	1.82	1.84
75°	4.7	3.37	3.36	1.68	1.73	2.19	2.19
75°	9.3	2.64	2.65	2.55	2.51	2.45	2.45
75°	13.8	2.31	2.32	2.97	2.99	2.53	2.51

Summary.

1. Acetaldehyde is oxidized in alkaline solution to acetic acid, oxalic acid and carbon dioxide.

2. The logarithm of the amount of acetic acid produced is a linear function of the logarithm of the alkali concentration between definite limits. Acetic acid production decreases as alkali concentration increases and as temperature increases.

3. These limits are a function of the temperature.

4. There is a minimum production of acetic acid at a concentration of alkali which is a function of the temperature. Increases in potassium hydroxide beyond this concentration has no appreciable effect upon acetic acid production.

5. The amounts of oxalic acid and carbon dioxide produced by the oxidation of acetaldehyde at a constant temperature are expressed as a mathematical function of the potassium hydroxide concentration between certain limits.

6. Since the production of these compounds is dependent upon those factors which decrease the amount of substance going to acetic acid, the same limits apply to the production of them as does to the production of acetic acid.

7. The ratio of oxalic acid to carbon dioxide increases with rise in temperature, and increase in alkali concentration. The amount of substance going to oxalic (or carbon dioxide) as compared to the total amount going to oxalic acid and carbon dioxide is a simple algebraic function of the alkali concentration.

8. The effect of the alkali on the yield of acetic acid should disappear at a temperature below 0°.

PART II.—THE OXIDATION OF ETHYLENE GLYCOL, GLYCOLLIC ALDEHYDE, GLYOXAL, GLYCOLLIC ACID AND GLYOXALIC ACID.

Historical Discussion.

The compounds ethylene glycol,[1] glycollic aldehyde,[2] glyoxal,[3] glycollic acid,[4] and glyoxalic acid,[5] and acetic acid are more or less readily transformed into each other by acid oxidizing or reducing agents.

As to the conduct of these compounds in the presence of bases the following reports are in the literature. Hydrogen is evolved and formic acid is formed when glycol is heated with lead peroxide and potassium hydroxide.[6]

Meyer and Jacobson in their text book[7] state that upon boiling, a *solution of glyoxal is changed over into a solution of glycollic acid.* Debus showed that upon boiling the solution of the calcium salt of glyoxalic acid, the salts of oxalic and glycollic acids were formed. Böttinger[8] showed that boiling the salt of the acid in the presence of potassium hydroxide caused the same reaction to take place. A basic barium glyoxalate is formed as an intermediate product during the action of barium hydroxide on glyoxalic acid. More prolonged action causes the evolution of hydrogen and the formation of oxalic acid.[1] Traube says that the quantity of hydrogen evolved is less in the experiments in which only small amounts of barium hydroxide were used.

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[1] Debus, *Ann.*, 110, 316 (1859); Renard, *Ann. Chim.*, [5] 17, 313 (1879).

[2] Neuberg and Schwenk, *Z. ver. Zuck.*, 1916, I, 430.

[3] Debus, *Ann.*, 102, 20 (1857).

[4] Würtz, *Ibid.*, 103, 366 (1857); Claus, *Ibid.*, 145, 256 (1868).

[5] Debus, *Ibid.*, 100, 1 (1856); 110, 316 (1859).

[6] Glaser and Morawski, *Monats.*, 10, 582 (1890).

[7] 2nd Ed., 1, 815 (1913).

[8] *Ber.*, 13, 1832 (1880).

To summarize these transformations in the presence of alkali it may be said that by the action of bases an intermolecular oxidation-reduction may be accomplished in the case of glyoxal and glyoxalic acid. It has also been shown that in two cases (glycol and glyoxalic acid) an alkali causes the evolution of hydrogen and the consequent oxidation of the compound to the alkali salt of oxalic acid.

Heimrod and Levene[2] have done considerable work upon the alkaline oxidation of glycol, glycollic aldehyde, glyoxal, glycollic acid and glyoxalic acid. Their method of experimentation was as follows:

A solution of the compound was made; to this was added varying amounts of a 4 *N* potassium hydroxide solution. A 30% hydrogen peroxide solution was added as an oxidizing agent. They analyzed the solution containing the oxidation products for total volatile acids (formic acid and carbon dioxide). They also tested for oxalic acid in the residue after the expulsion of the volatile acids. Large yields of formic acid and some carbon dioxide were obtained by the oxidation of glycol, glycollic aldehyde and glyoxal. Glycollic acid gave some glyoxalic acid, a larger amount of formic acid and over 50% yield of carbon dioxide.

The glyoxalic acid gave on oxidation large amounts of carbon dioxide and some oxalic and formic acids. Heimrod and Levene believe that the oxalic acid was produced by the action of the alkali on glyoxalic acid. They detected oxalic acid in a control experiment in which they used no hydrogen peroxide. In some of their experiments an excess of the oxidizing agent was used and in all others all of the hydrogen peroxide entered into reaction with the compound being oxidized. The temperature factor was not regulated and the yields were not quantitative.

Experimental Part.

Oxidations of glycol, glycollic aldehyde, glyoxal, glycollic acid and glyoxalic acid were conducted at a temperature of 50° in the same manner as described for acetaldehyde. The method of preparation of the compounds and the results of the oxidation of them are here given.

Ethylene Glycol.

Preparation of Ethylene Glycol.—The ethylene glycol was prepared from ethyl alcohol, through the intermediate formation of ethylene, ethylene dibromide, and glycol diacetate.

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[1] Traube, *Ber.*, **42**, 3295 (1909).

[2] *Biochem. Z.*, **29**, 31 (1910).

The Oxidation of Ethylene Glycol.—The oxidation of the ethylene glycol was carried out at an initial volume of 500 cc. The volume at the end of the oxidation was 525 cc.

The data obtained are given in the following table:

TABLE III.

G. $KMnO_4$.	G KOH per l.	G $(CH_2OH)_2$.	G $(COOH)_2$	G CO_2	G (CH_2OH) recovered as $(COOH)_2$ and CO_2	$(COOH)_2$ from 6 2 g $(CH_2OH)_2$	CO_2 from 6 2 g (CH_2OH_2)	Av g KOH per l
7 75	None	0 97	0 215	1 15	0 96	1 37	7 35	1 02
7.00	0 96	0 96	0 47	0 90	0 957	3 04	5 81	1 66
7.00	1.98	0 98	0 906	0 50	0 977	5 73	3 16	2 64
7.00	4 86	0 99	1 05	0 37	0 985	6 57	2 32	5 5
7.00	14.6	1 00	1 05	0 38	0 99	6 51	2 35	15 0
7.00	24 1	0 99	1.05	0 37	0 985	6 57	2 32	24 3
7.00	48 6	0 99	1 05	0 37	0 985	6 57	2 32	48 3

The amounts of oxalic acid and carbon dioxide which would be produced by the oxidation of 6.2 g. (0.1 Mol. wt.) of glycol under the conditions of the experiment are given in Cols. 6 and 7. These values plotted against the potassium hydroxide concentration are shown in Fig 6.

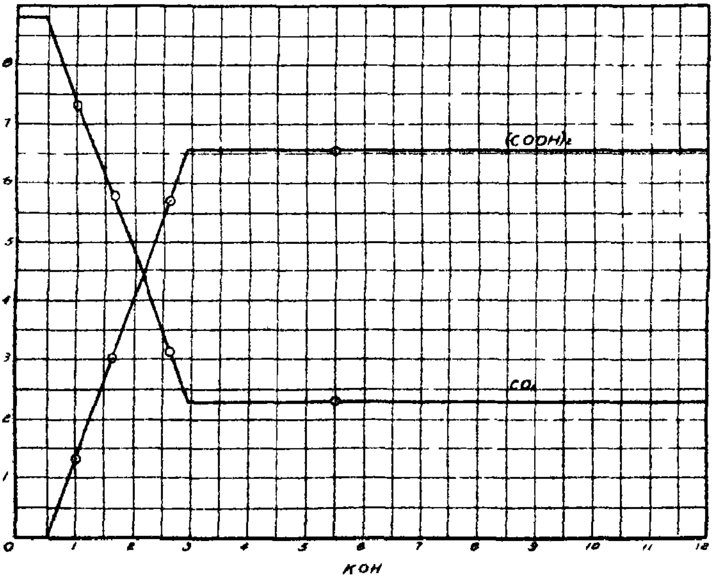


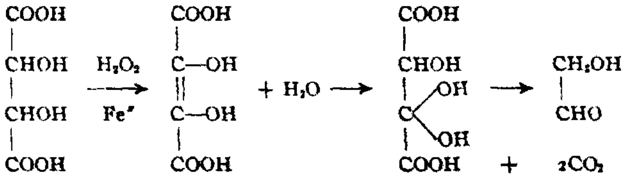
Fig. 6.—Glycol oxidations.

It may be seen that the amounts of these acids produced by the oxidation of a fixed amount of glycol constitute a linear function of the potassium hydroxide concentration between concentration of 0.5 g. and 3.0 g.

per liter. The equations showing these relationships are $Y_o = 2.73 X - 1.46$ and $Y_c = 10.13 - 2.64 X$, where Y_o equals the grams of oxalic acid, and Y_c the grams of carbon dioxide produced by the oxidation of a tenth molecular weight of glycol at a concentration of X g. of potassium hydroxide per liter. At concentrations below 0.5 g. of potassium hydroxide per liter it appears that glycol is oxidized quantitatively to carbon dioxide; at concentrations above the 3 g. per liter the ratio of the acids produced is not affected by changes in the concentration of potassium hydroxide. At concentrations above 3 g. per liter 73% of the glycol is oxidized to oxalic acid, and 27% to carbon dioxide.

Glycollic Aldehyde.

1. **Preparation.**—Three syntheses of glycollic aldehyde are reported in the literature. Fisher and Landsteiner[1] prepared a dilute solution from acetal. Marchwald and Ellenger[2] prepared a concentrated solution from α,β-dichloro-ethyl ether. Fenton[3] by the oxidation of a concentrated solution of tartaric acid with hydrogen peroxide in the presence of a small amount of ferrous iron prepared an acid which he showed to be dihydroxy maleic acid, $C_4H_4O_6.2H_2O$. This acid in cold aqueous solution slowly, and in warm solutions rapidly loses carbon dioxide and glycollic aldehyde is formed.



Dihydroxy-maleic acid was prepared by the Fenton method. From this a solution of glycollic aldehyde was prepared by dissolving a weighed amount of the crystallized dihydroxy maleic acid in water, which had been freed of oxygen. The decomposition of the acid was effected in an atmosphere of hydrogen at a temperature of about 70°. Carbon dioxide is rapidly evolved at this temperature. After expelling the carbon dioxide, the solution had a negligible acidity, gave the aldehyde reaction with Schiff's reagent, a silver mirror with ammoniacal silver nitrate, and a phenyl-osazone which melted at 169°. The phenyl-osazone of glyoxal melts at 169.5°.[4]

2. **The Oxidation of Glycollic Aldehyde.**—The oxidation was conducted in the usual manner. The data are given in the following table:

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[1] *Ber.*, 25, 2549 (1892).

[2] *Ibid.*, 25, 2984 (1892).

[3] *J. Chem. Soc.*, 65, 899 (1894).

[4] Pickel, *Ann.*, 232, 231 (1885).

TABLE IV.

G. $KMnO_4$	G. KOH per l.	G $C_2H_4O_2$.	G. $(COOH)_2$.	G. CO_2.	G $C_2H_4O_2$ recovered as $(COOH)_2$ and CO_2.	$(COOH)_2$ from 6 g. $C_2H_4O_2$	CO_2 from 6 g. $C_2H_4O_2$.	Av. g. KOH per l.
5.5	1.0	0.92	0.46	0.95	0.95	3.00	6.19	1.2
5.3	2.4	0.94	0.54	0.87	0.95	3.45	5.55	2.5
5.2	4.8	0.98	0.637	0.82	0.98	3.90	5.00	4.8
5.0	13.4	0.94	0.715	0.67	0.93	4.57	4.30	13.0

The amounts of oxalic acid and carbon dioxide produced by the oxidation of 6 g. (0.1 mol. wt.) of glycollic aldehyde are given in Cols. 6 and 7

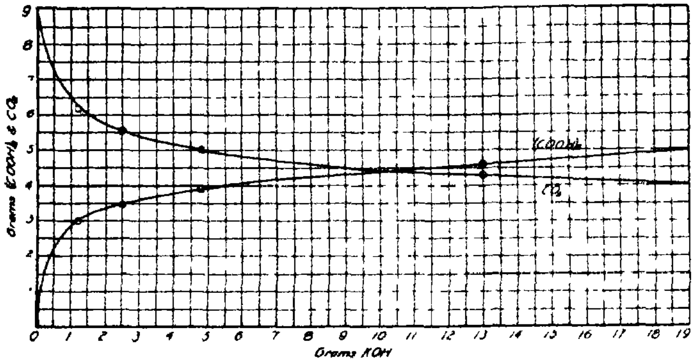

Fig. 7.—Oxidation of glycollic aldehyde.

and are plotted against the potassium hydroxide concentration in Fig. 7. The curve so obtained is a logarithmic one, for when the points are plotted

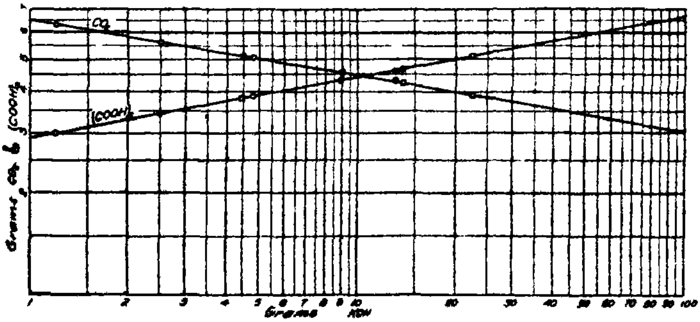

Fig. 8.—Oxidation of glycollic aldehyde.

on log paper a straight line is produced. This relationship is plotted on logarithmic paper in Fig. 8. The circled dots are the points experimentally determined.

Glyoxal.

1. The sodium acid sulfite derivative of glyoxal was used in this series of oxidations. Due to the comparative insolubility of the glyoxal bisulfite a standard solution was not prepared.

2. **The Oxidaticn of Glyoxal.**—The oxidation was carried out at a constant volume of one liter, the powdered bisulfite derivative being slowly added until the oxidizing solution was decolorized. The alkalinity at the end of the reaction was determined by titration, the average concentration of the potassium hydroxide being then calculated. The experimental results are given in Table V.

TABLE V.—OXIDATION OF GLYOXAL.

G $KMnO_4$	G KOH per l	G $(CHO)_2$	G $(COOH)_2$	G CO_2	G $(CHO)_2$ recovered as $(COOH)_2$ and CO_2	$(COOH)_2$ from 5 8 g $(CHO)_2$.	CO_2 from 5 8 g $(CHO)_2$	Av. g KOH per l
10 00	None	1 09	None	1 66		None	8 80	Acid
11 00	4 45	1 30	0 156	1 84	1 307	0 69	8 21	4 39
10 40	8 9	1 25	0 265	1 64	1 253	1 24	7 61	8.4
10 24	13 35	1 24	0 402	1 50	1 249	1 88	7 01	12 5
10 00	22 25	1.23	0 686	1 20	1 234	3.23	5 65	21 5
10 15	44 5	1 28	1 45	0 53	1 284	6 58	2 40	43 4
10 50	72 0	1 36	1 617	0 49	1 36	6 90	2 09	71.0
10 50	96 0	1.36	1 617	0 50	1 365	6 90	2 13	95.0

The amounts of oxalic acid and carbon dioxide which would be produced by 5.8 g. (0.1 mol. wt.) of glyoxal under the conditions of the experiment are given in Cols. 7 and 8. These values plotted against the concentration of potassium hydroxide per liter are shown in Fig. 9.

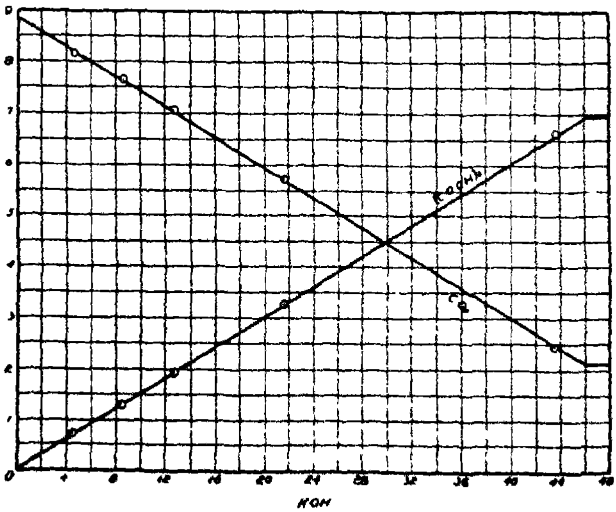

Fig. 9.—Oxidation of glyoxal

It may be seen that the amounts of these acids produced by the oxidation of a constant amount of glyoxal is a linear function of the potassium hydroxide concentration between the concentration of zero g. and 45.5 g. per liter. At concentrations above the latter figure changes in concentration of the potassium hydroxide produce no changes in the ratio of oxalic acid and carbon dioxide produced. Between these limits $Y_o = 0.151\ X$ and $Y_c = 8.8 - 0.145\ X$ where Y_o and Y_c represent the grams of oxalic acid, Y_c the grams of carbon dioxide produced by the oxidation of 5.8 g. of glyoxal at a concentration of X g. of potassium hydroxide per liter. At concentrations above 45.5 g. potassium hydroxide per liter 76.7% of the glyoxal is oxidized to oxalic acid.

Glycollic Acid.

Preparation of Potassium Glycollate, $\begin{matrix}CH_2OH\\ |\\ COOK.{}^1/_2H_2O\end{matrix}$.—Glycollic acid was prepared as by Witzemann.[1] The crystals of glycollic acid were washed and dried, dissolved in water, and neutralized with potassium hydroxide solution. After concentration of the solution on the water bath, the potassium glycollate crystallized out. The salt was recrystallized once.

The Oxidation of Glycollic Acid.—The oxidation of glycollic acid was carried out in the usual manner. The results are given in Table VI. The amounts of carbon dioxide and oxalic acid produced by the oxidation of 12.3 g. potassium glycollate are plotted against potassium hydroxide concentrations in Fig. 10.

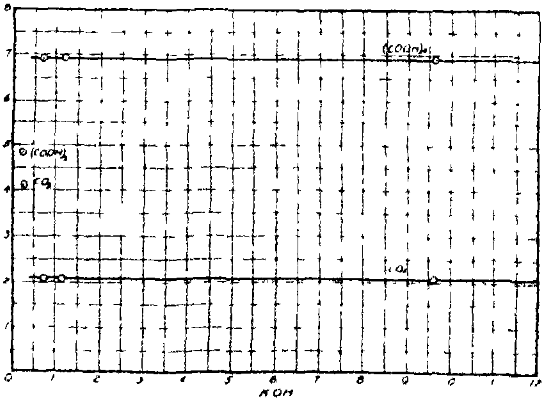

Fig. 10.—Oxidation of glyoxalic acid

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[1] This Journal, 39, 109 (1917).

TABLE VI.—OXIDATION OF GLYCOLLIC ACID

G $KMnO_4$	G KOH	$(C_2H_3O_3K)$ $^1/_2H_2O$	G $(COOH)_2$	G CO_2	G $C_2H_3O_3K.^1/_2H_2O$ recovered as $(COOH)_2$ and CO_2	$(COOH)_2$ from 12 3 g of the salt	CO_2 from 12.3 g. of the salt	Av g KOH per l
2 00	None	1 05	0 41	0 35	1 057	4 80	4 10	0 23
2 00	0 43	1 05	0 59	0 18	1 053	6 90	2 09	0 68
2 10	0 96	1 18	0 664	0 20	1 182	6 91	2 07	1 11
2 10	9 6	1 23	0 695	0 205	1 233	6 95	2 05	9 6
2 10	48 0	1 23	0 69	0 21	1 232	6 90	2 10	47 0

The same percentage of potassium glycollate is oxidized to oxalic acid regardless of whether the initial concentration of potassium hydroxide is 0.68 g. or 48 g. per liter

It is only in the solution to which no potassium hydroxide was added that a less percentage of the oxalic acid is produced. The average concentration of potassium hydroxide in the "neutral solution" would be 0 23 g , for the amount of potassium hydroxide produced by the hydrolysis of potassium permanganate and by the potassium glycollate is in excess of the amount needed to neutralize the acids

Glyoxalic Acid.

Preparation of Potassium Glyoxalate.—Potassium glyoxalate was prepared by the method of Otto Bechurts [1] The salt was recrystallized from water and alcohol.

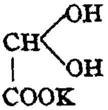
Oxidation of Potassium Glyoxalate.—The results obtained by the oxidation of  $CH(OH)_2COOK$ are given in Table VII.

TABLE VII.—OXIDATION OF GLYOXALIC ACID

G $KMnO_4$.	G KOH per l	G $C_2H_3O_4K$	G $(COOH)_2$	G CO_2	G $C_2H_3O_4K$ recovered as $(COOH)_2$ and CO_2	$(COOH)_2$ from 13 g salt.	CO_2 from 13 g salt	Av conc. KOH per l.
1 2	None	0 80	None			.	8 80	Acid
1 2	0 50	1 24	0 403	0 44	1 231	4 22	4 61	0 47
1 2	0 99	1 24	0 43	0 41	1 227	4 50	4 30	0.93
1 2	2.4	1 20	0 453	0 36	1 185	4 91	3 90	2 1
1 2	4 9	1 20	0 50	0 32	1 193	5 42	3.47	4 6
1 2	4 8	1 30	0 624	0 26	1 293	6.35	2.64	45.0

The amounts of oxalic acid and carbon dioxide which would be produced by the oxidation of 13 g. (0.1 mol. wt.) of potassium glyoxalate are given in Cols. 7 and 8 of the table and are plotted against the average potassium hydroxide concentration in Fig. 11 and on logarithmic paper in Fig. 12. The logarithm of the oxalic acid and carbon dioxide production is a linear function of the logarithm of the potassium hydroxide concentration. The mathematical expression of this is $Y_o = 4.55\ X^{0.1087}$ and

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[1] *Ber*, 14, 581 (1881).

$Y_c = 4.28\ X^{-0.1377}$ Y_o equals g. of oxalic acid and Y_c g. of carbon dioxide produced by the oxidation of 13 g. of potassium glyoxalate at a concentration of X g. of potassium hydroxide per liter.

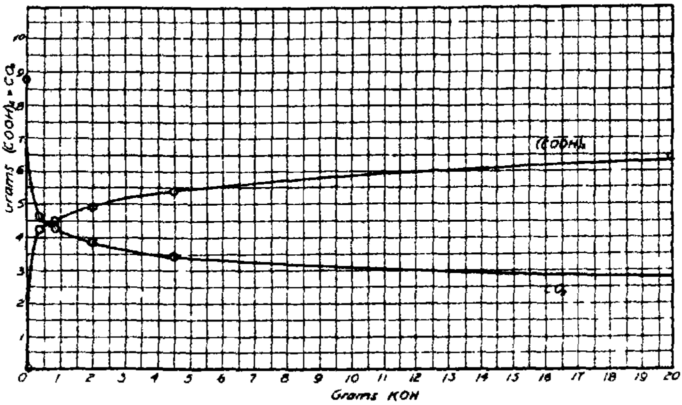

Fig. 11.—Oxidation of glyoxalic acid.

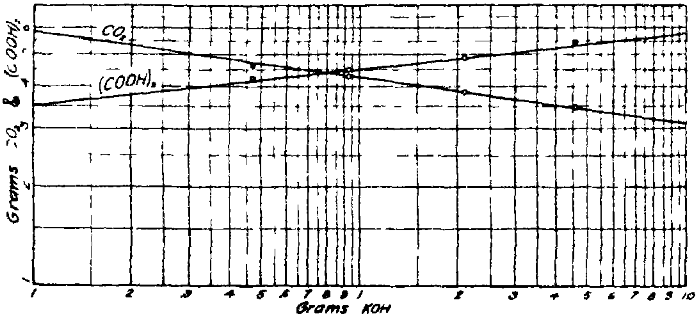

Fig. 12.—Oxidation of glyoxalic acid

Discussion of Results.

1. The compounds whose oxidation products have here been studied may be classified in a number of ways One way which is rather suggestive is on the basis of the similarity of the groups in the molecule.

A. Acetaldehyde, glycollic aldehyde, glyoxalic acid, glycollic acid would be classified together on this basis for the groups within the molecule are dissimilar. In the first compound there is a methyl group and an aldehyde group, in the second an alcohol group and an aldehyde group, in the third an aldehyde group and a carboxyl group, in the fourth an alcohol group and a carboxyl group.

B. In glycol and glyoxal, the two carbons in each compound hold the same groups, hence are classified together.

2. The relationship of the potassium hydroxide concentration to the amount of the oxidation products of group A is markedly different from the relationship which it bears to the oxidation products of the compounds of group B. The logarithms of the weights of the oxidation products of group A are (with the *possible* exception of glycollic acid) linear functions of the logarithms of the potassium hydroxide concentration employed. The amounts of the oxidation products of group B are linear functions of the potassium hydroxide concentration. Ethyl alcohol would be in group A for in this compound dissimilar groups are attached to the two carbon atoms.

3. In Fig. 8 the amounts of oxalic acid and carbon dioxide which are obtained by the oxidation of $^1/_{10}$ the molecular weight of glycollic aldehyde at various concentrations of potassium hydroxide are plotted. The experimental points on this line are circled. In this same graph the points within the squares represent the figures given in Col. 9 of acetaldehyde Table I for 50°. It may be seen by reference to the description of the method for deriving these figures that they represent the weights of oxalic acid which are produced by the oxidation of $^1/_{10}$ of the molecular weight of the substance which is oxidized to oxalic acid and carbon dioxide during the alkaline oxidation of acetaldehyde. As may be seen the points within the squares lie on the same straight line as the points within the circles. This means that the potassium hydroxide has the same effect on the intermediate compound formed in the alkaline oxidation of

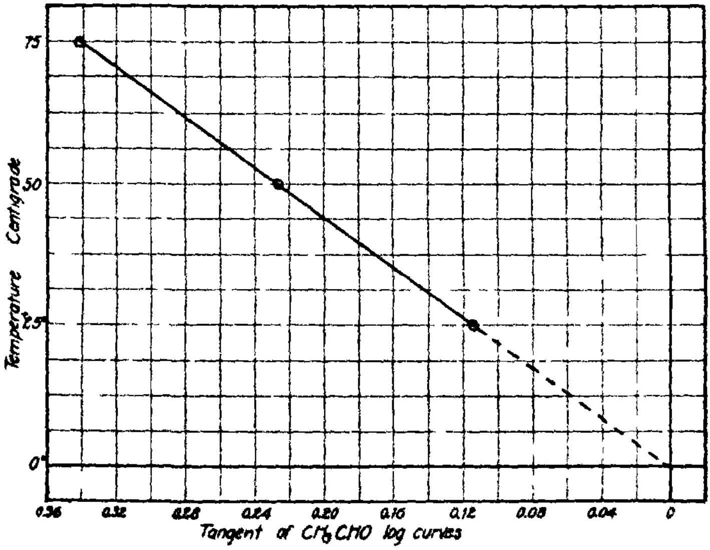

Fig 13

acetaldehyde as it does upon glycollic aldehyde when the latter compound is oxidized in alkaline solution with potassium permanganate. This identity of effect may be shown in another way. If glycollic aldehyde is the intermediate product in the oxidation of acetaldehyde then the equations which were derived for the production of oxalic acid and carbon dioxide from the intermediate product should hold true for the production of these compounds from glycollic aldehyde. The equations derived for 50° were as follows:

$$Z_o = 2.87\, X^{0.184} \qquad (1)$$

$$Z_c = 6.5\, X^{-0.165} \qquad (2)$$

where Z_o is the weight of the oxalic acid; Z_c, the weight of the carbon dioxide; and X, the weight of the potassium hydroxide per liter.

The correlation of the weights of the oxidation products obtained from glycollic aldehyde experimentally and those calculated by means of the two above equations is shown in the following table:

TABLE VIII.—GLYCOLLIC ALDEHYDE OXIDATION. RESULTS CALCULATED AND OBSERVED.

Value of X G. per l.	G. of oxalic acid.		G. of carbon dioxide.	
	By expt.	By calculation.	By expt.	By calculation.
1.2	3.00	2.97	6.19	6.30
2.5	3.45	3.40	5.55	5.60
4.8	3.90	3.83	5.00	5.02
13.0	4.57	4.60	4.30	4.25

This shows that these equations do express within the limits of experimental error the relationship of the alkali concentration to the amounts of oxidation products.

This, then, is strong evidence in favor of the theory of Nef and Denis that glycollic aldehyde is an intermediate compound formed in the alkaline oxidation of acetaldehyde with potassium permanganate.

McLeod[1] has shown that vinyl alcohol molecules are present in a solution of acetaldehyde as soon as a concentration of 0.1% of alkali is attained. It is shown in Part I that the oxidation of acetaldehyde to acetic acid is not quantitative when the potassium hydroxide concentration is greater than about 0.1%. That is, oxalic acid and carbon dioxide begin to be formed by the alkaline oxidation of acetaldehyde as soon as the alkali concentration reaches a point which is approximately the same as that which McLeod has shown to be the concentration at which the formation of vinyl alcohol molecules first occurs. The present paper also shows that potassium hydroxide concentration has the same effect upon the intermediate compound in the oxidation of acetaldehyde as it does upon glycollic aldehyde, and that it behaves in an entirely different manner upon the other two carbon atom compounds which have been studied.

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[1] *Loc. cit.*

4. It may be seen by reference to the tables that the maximum amount of oxalic acid produced by the oxidation of $^1/_{10}$ the molecular weight of glyoxal is the same as the maximum amount produced by the oxidation of $^1/_{10}$ the molecular weight of potassium glycollate. A concentration of 45.5 g. of potassium hydroxide per liter is required in the case of glyoxal while in the case of potassium glycollate less than one gram is required.

Glyoxal on being boiled in aqueous solution is converted into glycollic acid. Benzoyl formaldehyde does not undergo the benzilic acid rearrangement in hot water, but in cold alkaline solutions this change takes place with such remarkable speed to form mandelic acid that Fehling's solution is unaffected by this keto-aldehyde. The effect of the alkali on glyoxal is to cause this compound to undergo the benzilic acid rearrangement to glycollic acid. Consequently, the amount of oxalic acid produced by the oxidation of glyoxal should be the same as the maximum amount produced by the oxidation of glycollic acid.

5. The effect of the alkali concentration on the production of oxalic acid and carbon dioxide from glycol, glycollic aldehyde, glyoxal, glycollic acid and glyoxalic acid under the conditions of these experiments is seen to be widely different within certain limits in the compounds studied. Considerable light is shed on the course of the oxidation of these compounds when the relationships of the graphs are studied.

A. Glycol.—The production of oxalic acid and carbon dioxide from glycol reaches a constant value when the concentration of the alkali is 3 g. per liter; from glycollic acid at a concentration lower than that for glycol; from glyoxal at a concentration of 46 g. per liter.

Nef,[1] made a study of the behavior of certain glycols and glycerol towards alkalies alone and towards alkaline oxidizing agents. He found that hydrogen, ethyl alcohol, carbon dioxide, formic acid, acetic acid and glycollic acid were obtained by heating a mixture of ethylene glycol and sodium hydroxide for 2.5 hours at 230° to 285°.[2] As noted above glycol reacts with aqueous solutions of alkalies containing lead peroxide giving hydrogen as one of the products. This result in aqueous solution is in harmony with the pyrogenic decomposition of glycol.[3]

The presence of carbon dioxide in our experiments with glycol and also those of Glaser and Morawski[3] can be readily explained on the assumption

[1] *Ann.*, 335, 279 (1904).

[2] Cf. Wurtz, *Ann. chim. phys.*, [3] 55, 417, 477 (1859).

[3] *Loc. cit.*

of the intermediate formation of glycollic aldehyde which is immediately dissociated into two molecules of formaldehyde,[1] *i. e.*,

$$(a)\ CH_2OH.CH_2OH \longrightarrow CH_2OH.CHO \longrightarrow 2CH_2O.$$

In harmony with Nef's views to the effect that the metallic salts of the alcohols dissociate at lower temperatures than the alcohol itself, it is evident that as the concentration of the alkali increases in these oxidations, the tendency of the glycol would be towards the formation of glyoxal, *i. e.*,

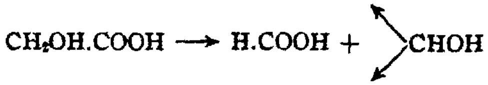
$$CH_2OH.CH_2OH \longrightarrow CHO.CHO + 2HOH.$$

As we have repeatedly pointed out, glyoxal is converted to glycollic acid even in the cold in aqueous alkalies. This reaction is so rapid in Fehling's solution that no reduction whatsoever takes place.[2]

If glycol reacts to give compounds which yield carbon dioxide on oxidation, and furthermore if glycol reacts to give glycollic acid as an intermediate compound, then it follows since glycol and glycollic acid are both oxidized to carbon dioxide and oxalic acid under the same conditions, the yield of carbon dioxide should be greater and that of the oxalic acid should be less than the yield of these two compounds would be from glycollic acid. That this explanation of the oxidation of glycol is the correct one is very evident from Figs. 6 and 10.

The only glyoxal which we had at our disposal was that obtained from the sodium acid sulfite compound obtained from Kahlbaum. Harries and Temme[3] have pointed out the existence of several polymerized forms of glyoxal which reduce Fehling's solution while the monomolecular variety does not. From our general knowledge of the behavior of monomolecular glyoxal and like compounds towards alkalies, it is evident that Fig. 10 would also be that for monomolecular glyoxal. From these facts it is obvious that Fig. 9 must be that of one of the polymeric varieties of glyoxal.

B. Glycollic Acid.—That glycollic acid is the intermediate compound in the oxidation of glycol which in turn is oxidized to carbon dioxide and oxalic acid follows from a consideration of Figs. 10 and 12. If glyoxalic acid were such an intermediate compound then the amounts of oxalic acid and carbon dioxide produced would not become constant at concentrations of alkali as low as one gram per liter. Glycollic acid may be supposed to react as follows:

(a) 

$$(a)\ CH_2OH.COOH \longrightarrow H.COOH + \rangle CHOH$$

which would yield carbon dioxide, and

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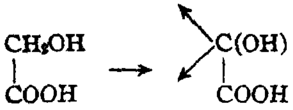
[1] Cf. Nef, *Ann.*, 335, 312 (1904).

[2] Debus, *Ibid.*, 100, 5 (1856); *Ibid.*, 102, 20 (1857).

[3] *Ber.*, 40, 165 (1907).

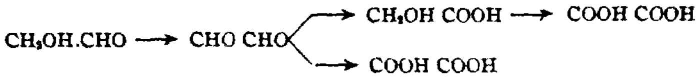
(b)



$$\begin{array}{l}\mathrm{CH_2OH}\\ |\\ \mathrm{COOH}\end{array} \longrightarrow \begin{array}{l}\nwarrow\\ >\mathrm{C(OH)}\\ \swarrow\ |\\ \mathrm{COOH}\end{array}$$

which on oxidation would give oxalic acid.

Glycollic Aldehyde.—Since it has been firmly established by the above work that glycollic aldehyde is an intermediate product in oxidation of acetaldehyde to oxalic acid and carbon dioxide it is of the greatest interest to trace the course of this oxidation if possible to the intermediate compound just preceding the formation of oxalic acid and carbon dioxide. Heimrod and Levene,[1] Witzemann[2] and Denis[3] explain the oxidation of glycollic aldehyde on the basis that this compound is oxidized to glyoxal and this in turn to oxalic acid, *i. e.*,



$$\mathrm{CH_2OH.CHO} \longrightarrow \mathrm{CHO\ CHO}\begin{cases}\longrightarrow \mathrm{CH_2OH\ COOH} \longrightarrow \mathrm{COOH\ COOH}\\ \longrightarrow \mathrm{COOH\ COOH}\end{cases}$$

If glyoxal is formed in the alkaline oxidation of glycollic aldehyde, then the intermediate formation of glycollic acid is to be expected by the reaction of glyoxal with alkalies.

A second possibility is that the alcohol and the aldehyde group of glycollic aldehyde undergo simultaneous oxidation with the formation of glyoxalic acid. A third possibility is that the aldehyde group of glycollic aldehyde is oxidized to a carboxyl group with the formation of glycollic acid. The experimental evidence presented in this paper does not offer conclusive evidence as to the exact course of the reaction in the alkaline oxidation of glycollic aldehyde.

Summary.

1. The production of oxalic acid and carbon dioxide from glycol and polymeric glyoxal in the alkaline oxidation with potassium permanganate is a linear function between certain definite limits of the potassium hydroxide concentration in the oxidizing media.

2. The logarithm of the production of oxalic acid and carbon dioxide from glycollic aldehyde and glyoxalic acid (and probably from glycollic acid) is a linear function between certain limits of the logarithm of the potassium hydroxide concentration in the oxidizing media.

3. Very strong experimental evidence is given to show that glycollic aldehyde is formed as an intermediate product in the alkaline oxidation of acetaldehyde with potassium permanganate.

4. Evidence is presented to show that potassium permanganate in alkaline solution oxidizes the two carbon alcohols, aldehydes and acids according to the following scheme:

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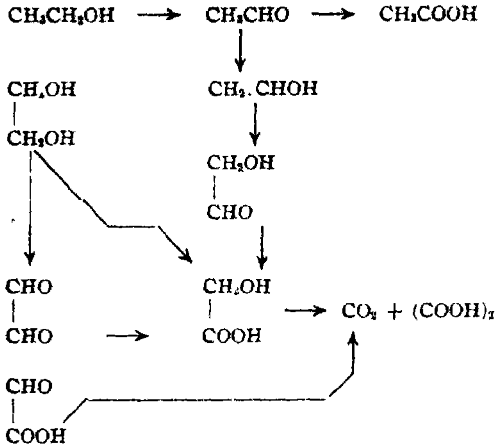
[1] *Biochem. Z.*, 29, 31 (1910).

[2] THIS JOURNAL, 39, 2657 (1917).

[3] *Am. Chem. J.*, 38, 568 (1907).



COLUMBUS, OHIO

ETHYLENE CHLOROHYDRIN AND β,β-DICHLOROETHYLSULFIDE.[1]

By M. Gomberg.

Received June 21, 1919

Within a few days after the so-called "mustard gas" was introduced as a means of offence in warfare (July 12-13, 1917), it was definitely identified as β,β-dichloroethylsulfide. There was reason to believe that it had been manufactured from ethylene chlorohydrin, according to the method described some 30 years previously by V. Meyer.[2] A second possible method,—the reaction between ethylene and the mono- or dichloride of sulfur,—was also given some consideration, but on the basis of preliminary experiments in several laboratories, was not looked upon at that time as promising.[3]

The directions in the literature for the preparation of dichloroethylsulfide from chlorohydrin seemed sufficiently explicit to furnish the basis of a reliable technical process. The reactions are as follows: (1) Ethylene chlorohydrin, in solution, reacts with sodium sulfide and gives dihydroxyethylsulfide in good yields; (2) this product, harmless in itself, gives the highly toxic dichloroethylsulfide when treated with phosphorus pentachloride (V. Meyer) or with conc. hydrochloric acid.[1]

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[1] This article has been approved for publication by the Director of the Chemical Warfare Service. The experimental work was done at the Chemical Laboratory, University of Michigan, under the auspices of the Bureau of Mines, War Gas Investigations. The results were reported to the Bureau of Mines in three reports—March 9, April 8, and June 28, 1918.

[2] *Ber.*, 19, 3260 (1886).

[3] In the light of subsequent and the more recent events, it seems almost certain that Guthrie actually did have in his hands some dichloroethylsulfide, as a result of his experiments with this reaction. He says: "Its smell is pungent and not unpleasant, resembling that of oil of mustard; its taste is astringent and similar to that of horse-radish. The small quantities of vapor which it diffuses attack the thin parts of the skin, as between the fingers and around the eyes, destroying the epidermis. If allowed to remain in the liquid form on the skin, it raises a blister." (*Quart J. Chem. Soc.*, 12, 117 (1860).)

$$2HOCH_2CH_2Cl + Na_2S = HOCH_2CH_2 - S - CH_2CH_2OH + 2NaCl.$$

$$(HOCH_2CH_2)_2S + 2HCl = ClCH_2CH_2 - S - CH_2CH_2Cl + 2H_2O.$$

The fundamental difficulty was how to get the chlorohydrin itself. The methods in the current scientific literature for the preparation of this substance seemed wholly inadequate for a technical process. These methods fall within two classes: (*a*) the addition of hypochlorous acid to ethylene,[2] (*b*) the action of sulfur monochloride,[3] of hydrochloric acid,[4] or of chlorine[5] upon pure ethylene glycol. For the preparation of chlorohydrin merely on a laboratory scale it has been found more desirable to use pure ethylene glycol,—in itself not readily obtainable,—as the starting point, and this is the method usually recommended. But from the practical standpoint, for a technical method, the hypochlorous acid addition reaction seemed to offer more promise, notwithstanding the discouraging facts that alkaline hypochlorites as such are known to have no action on ethylene, that free hypochlorous acid can only be prepared in solutions from 1 to 3%, and that the best yield of chlorohydrin by this reaction was known to be only about 30% of the theoretical amount (Butlerow).

The most feasible source of hypochlorous acid for technical operation was deemed to be bleaching powder. It was suggested, in various reports from abroad that ethylene could be passed into a suspension of bleaching powder in water, and dil. mineral acid, or carbon dioxide under pressure, could be used to liberate hypochlorous acid at the rate that the latter is being used up by the ethylene. Whether chlorohydrin has actually been made by the above method on a technical scale, the writer does not know. Our own experience in this direction on laboratory scale gave poor yields of chlorohydrin.

In view of the many difficulties connected with the use of bleaching powder, several investigators independently of each other attempted to utilize as the source of hypochlorous acid the solution of chlorine in water, *i. e.*, bringing chlorine and ethylene into reaction in presence of water. As is well known, the reaction between chlorine and water yields but very little hypochlorous acid. This is due not merely to the inherent proneness of the acid towards decomposition with liberation of oxygen, but even more so to the presence of the hydrochloric acid.

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[1] H. T. Clarke, *J. Chem. Soc.*, 101, 1583 (1912).

[2] Carius, *Ann.*, 126, 197 (1863); Butlerow, *Ibid.*, 144, 42 (1867).

[3] Carius, *Ibid.*, 124, 257 (1862); Fittig u. Ström, *Ibid.*, 267, 191 (1892).

[4] Ladenburg, *Ber.*, 16, 1407 (1883).

[5] Donciu, *Monatsh.*, 16, 3 (1895).

$$Cl_2 + H_2O \rightleftharpoons HCl + HOCl.$$

The equilibrium is thus very much on the left-hand side of the equation. Consequently, it was generally assumed that since the amount of hypochlorous acid as compared with the amount of free chlorine must at best be but small, the tendency would therefore be greater towards the formation of ethylene chloride rather than of chlorohydrin

$$CH_2{:}CH_2 + HOCl = HOCH_2.CH_2Cl.$$
$$CH_2{:}CH_2 + Cl_2 \quad = ClCH_2.CH_2Cl.$$

Various procedures were suggested in order, presumably, to obviate, or to overcome this difficulty. Some[1] have proposed to pass ethylene and chlorine into a solution of sodium borate,—the borax, through its interaction with the hydrochloric acid, should keep down the hydrogen ion concentration; sodium hydroxide is added at intervals in order to bring back into solution the boric acid which has separated. Others have used copper oxy-chloride, alternately saturating the solution with chlorine and with ethylene, catalytic influence being claimed as additional advantage for the copper salt.[2] Some[3] have proposed to pass the unsaturated hydrocarbon into an aqueous bath in which "chlorine or hypochlorous acid is generated electrolytically." Others[4] have carried on the reaction between ethylene and chlorine in presence of steam, or at temperatures slightly under 100°, introducing the two gases simultaneously or alternately. Obviously, of the procedures mentioned above, only those that employ borax or copper oxychloride actually tend to depress the hydrogen ion concentration[5] and thus do affect the equilibrium in favor of the hypochlorous acid, and, presumably, in favor of chlorohydrin But, as will be shown in this paper, the accumulation of the sodium chloride in solution is more harmful than that of hydrochloric acid and is distinctly detrimental to the favorable progress of the reaction. The procedures based upon the interaction of ethylene, chlorine and water at, or near to, 100° can hardly favor the reaction between chlorine and water in favor of hypochlorous acid. In all probability they give lower yields of chlorohydrin,—the hypochlorous acid is less stable at that temperature, the ethylene is less soluble, etc. The surmised advantage of such methods is that chlorohydrin is being removed from its dil. aqueous solution as soon as produced, by virtue of the fact that it tends to form with water a constant boiling mixture possessing a low boiling point, as will be shown further on. But chlorohydrin of itself is of least influence as a factor in depressing the concentration of the desired product attainable in this reaction, which also will be shown later.

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[1] J. B. Conant, in report to the Bureau of Mines Williamson, in 1845, used disodium acid phosphate (*Ann.*, **54**, 133 (1845)).

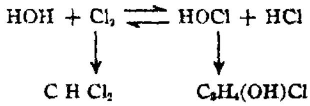
[2] J. C. Irvine, of St. Andrews University, in report at Bureau of Mines.

[3] McElroy, *U. S. pat.* 1,253,615, *C. A.* **12**, 702 (1918).

[4] E. P. Kohler, in report to the Bureau of Mines; McElroy, *U. S. pat.* 1,253,616, *C. A.* **12**, 703 (1918); Commerc. Research Co., *Br. pats.* 113,954 and 113,955, *C. A.*, **12**, 1469 (1918); Eldred, *Can. pat.* 186,634, *C. A.*, **12**, 2325 (1918).

[5] It must not be forgotten that by the use of those bases which produce soluble chlorides the concentration of the hydrogen ion is depressed, but not that of the chlorine ion. Hence, the improvement due to the use of such bases is limited. See Jakowkin, *Z. physik. Chem.*, **29**, 613 (1889).

The premises which the writer used for the working out of his procedure were of somewhat different nature from those as above described.[1] They were suggested by the excellent paper by John Read and Margaret M. Williams,[2] on the action of bromine water on ethylene. Substituting chlorine for bromine we can express, as they have done, the relationship between water, chlorine and ethylene schematically in the following manner.



$$\begin{tikzcd}[column sep=small] HOH + Cl_2 \arrow[r, shift left, harpoon] \arrow[d, shift right=8] & HOCl + HCl \arrow[l, shift left, harpoon] \arrow[d, shift left=8] \\ C\ H\ Cl_2 & C_2H_4(OH)Cl \end{tikzcd}$$

In other words, the principal factor which is likely to determine the ratio of ethylene chloride to chlorohydrin must lie, after all, in the relative velocities of the two reactions,—between ethylene and chlorine on the one hand, and between ethylene and hypochlorous acid on the other. In case the second reaction occurs with greater velocity than the first, then we should be dealing with a case of mobile equilibrium, and the principal product would be chlorohydrin,—provided that care be taken to maintain stirring, so that ethylene reacts only with the chlorine in solution and not with the gaseous chlorine. Experiments proved that such is actually the case. Very little ethylene chloride is produced until a concentration of 6 to 8% of chlorohydrin has been attained.

A brief study has been made of some factors which influence the rate of chlorohydrin formation, the concentration of chlorohydrin attainable, also of the practical means of separating the chlorohydrin from its aqueous solution. Some data concerning the preparation of β,β-dichloroethylsulfide from chlorohydrin, and of unsuccessful attempts to prepare it from ethylene chloride, are given at the end of this paper.

I. Chlorohydrin.

Ethylene.—The unsaturated hydrocarbon was prepared from alcohol by the use of aluminum sulfate as the catalyst.[3] The hydrated aluminum salt was heated in an iron dish till the water was driven off The porous residue was granulated, the larger lumps reduced to about $^1/_8$ inch in diameter, and the fine powder was removed by sifting through a 20-mesh sieve. The granular salt was placed in a 30-inch brass tube through a length of about 25 inches, and the tube placed in an electrically heated furnace. The alcohol was led into the tube in the form of vapor, previous preheating of the vapor having been found to be without advantage in our small scale experiments. The issuing gases were passed through a condenser and receiver and collected as usual over water. Best results were obtained with a temperature of 420 to 460°. The yield of ethylene varied, 60 to 80% of the calculated amount being produced. The ethylene is 95 to 97% pure. The aluminum sulfate gradually becomes reduced and at the same time coated with a layer of carbon, but on reheating in the furnace and passing air over it, the catalyst becomes white and resumes its former activity.

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[1] None of the above mentioned processes was known to the writer at the time his own work was being done.

[2] *J. Chem. Soc.*, 111, 240 (1917).

[3] Sabatier and Mailher, *Ann., chim. phys.*, [8] 20, 300 (1910); Senderens, *Ibid.*, 25, 491 (1912).

Procedure.—From one to three liters of water was placed in a wide-mouth bottle which was provided with a tightly fitting stopper with 4 holes. One opening carried a glass tubing for the introduction of ethylene; the second, for the introduction of chlorine; the third is for an efficient stirrer, and the fourth carried a tube for connection with a trap, in order to indicate whether any uncombined gas was escaping,—ethylene or chlorine, and also for the purpose of carrying on the reaction under slight pressure when this was desired. The rate at which the gases were introduced was carefully noted, and the relative quantities of each were so regulated that practically no gas left the reaction chamber. The ethylene was kept just enough in excess over chlorine to keep the solution colorless. At the end of the experiments the aqueous solution was separated from the ethylene chloride if any had been formed, and the amount of chlorohydrin in solution was carefully determined in an aliquot portion. The method of estimation is based upon the difference between the indices of refraction of water (1.333) and pure chlorohydrin (1.442). The indices of refraction of known concentrations of chlorohydrin were determined in an Abbe refractometer, and plotted, the result being a straight line. In order, therefore, to determine the quantity of chlorohydrin in a given solution, some of the latter is carefully neutralized with sodium carbonate and distilled. From the index of refraction of the distillate, previously diluted in order to throw out any ethylene chloride that might be present in solution, the per cent. of chlorohydrin in the distillate is read off at once. The method is rapid and readily accurate within 0.5%.

Rate of Formation, and the Concentration Attainable.—The rate at which the gases could be introduced was found to depend very much upon the efficiency of the stirring arrangement. At the outset of the operation they were often passed in at the rate of 20 to 25 liters each per hour, the solution being kept at about 10 to 12°, which gave almost as good results as 0°. But such rates cannot be kept up for long, and with the progress of the reaction the rate of combination between the two gases slows down. Up to a concentration of chlorohydrin equal to 5%, and 2.5% hydrochloric acid, there is hardly any ethylene chloride being formed. But when the concentration of chlorohydrin has reached about 8% the absorption of the reacting gases becomes markedly slower, even when employing vigorous stirring and working under a pressure of 2 to 3 inches mercury. But by continuing to pass in the gases at a slow rate it is possible to attain concentrations of chlorohydrin equal to 14 to 15%. Such high concentrations are reached, however, only at the expense of a good deal of ethylene, since with the increase of concentration in chlorohydrin proportionately more and more ethylene chloride is produced.

Salts of mercury, because of their capacity to unite with ethylene, were tested as possible favorable catalysts for this reaction. The results, however, did not indicate any particular influence in this respect.

Effect of Neutralizing the Acid.—The attempt to depress the amount of hydrochloric acid, which might otherwise accumulate in the reaction mixture, by the addition of powdered marble or precipitated calcium carbonate resulted unfavorably. The aqueous solution soon became saturated with carbon dioxide; this, apparently, greatly diminished the solubility of ethylene, and after a while the reaction slowed down very considerably. Much better results were obtained when the neutralization was done at intervals by successive small additions of calcium hydroxide in amounts corresponding to the quantity of the acid formed, as judged from the amount of ethylene used up. By this procedure solutions containing 14 to 15% of chlorohydrin were obtained. Thus, the neutralization of the acid is of little effect as regards the concentration of chlorohydrin attainable. Nor was there any evidence that the rate of reaction was improved, on the contrary, it rather seemed as if the rate of combination was somewhat slower than when the acid was left unneutralized, which effect might have resulted from the probable decrease in solubility of the gases in water containing calcium chloride, or any other salts, for that matter.

Ratio between Chlorohydrin and Ethylene Chloride.—It was found that when the operation is limited to the production of only 6 to 8% of chlorohydrin there is comparatively little ethylene chloride produced, from 0 to 10%. Higher concentrations, particularly 14 to 15%, are obtained, as indicated above, only by using a good deal of ethylene, which is lost in the formation of ethylene chloride. When ethylene, chlorine and water alone are used, the by-product is hydrochloric acid; if this acid is progressively neutralized with borax, sodium hydroxide, or calcium hydroxide, the corresponding salts are produced. Experiments were carried out with the object of getting some idea as to the influence which these various products exert on the ratio of chlorohydrin to ethylene chloride, *i. e.*, the influence of chlorohydrin, of hydrochloric acid, and of the different salts. As has been mentioned, very little ethylene chloride is ordinarily produced when the concentration of chlorohydrin is 8% or lower, *i. e.*, when the concentration is equal to a *N* solution or less. Under these circumstances, the concentration of the acid, or of the salts resulting on its neutralization, is approximately similar. Obviously, then, the pronounced influence of each of the factors mentioned comes into play only after the normal concentration is reached, as not until then does the formation of ethylene chloride commence to be appreciable. Accordingly, the experiments were arranged in this manner: One liter of water was taken, chlorine and ethylene passed into it, and at intervals the content of chlorohydrin and ethylene chloride produced was determined; this was continued until the concentration of the former was considerably above normal. Then experiments under as nearly similar conditions as possible were carried out, with water which contained, to begin with, an amount of chlorohydrin, or of acid, or of the salts, to make *N* or 2 *N* of each, respectively. The following table gives the results obtained. The initial strength of the various solutions, as well as the concentration of the

TABLE I.

	Chlorohydrin produced		Ethylene dichloride		Ethylene distribution.	
Solution	Concentration *N*	Ethylene consumed G.	Cc	Ethylene consumed. G.	In chlorohydrin %.	In ethylene chloride %.
Water..........	0.92	25.8	0.0	0.0	100	0
	1.25	35.0	10.0	3.62	91	9
	1.62	45.4	22.0	7.96	85	15
Chlorohydrin, *N*	0.92	25.8	1.0	0.36	99	1
Chlorohydrin, *N*...	0.54	15.1	0.0	0.0	100	0
	0.63	19.0	3.5	1.27	94	6
Hydrochloric acid, 2 *N*.....	0.23	6.44	0.0	0.0	100	0
	0.47	13.20	2.0	0.72	96	4
	0.94	26.40	12.0	4.35	86	14
Hydrochloric acid, 2 *N*......	0.40	11.2	1.0	0.36	97	3
	0.69	19.3	8.0	2.90	87	13
Calcium chloride, 2 *N*.....	0.46	12.9	7.0	2.53	84	16
	0.75	21.0	17.0	6.15	77	23
	1.04	29.1	36.0	13.00	69	31
Calcium chloride, 2 *N*.....	0.40	11.2	9.0	3.26	77	23
	0.69	19.3	18.0	6.52	75	25
	0.96	26.9	34.0	12.50	70	30
Magnesium chloride, 2 *N*....	0.43	12.1	3.5	1.27	90	10
	0.66	18.5	18.0	6.52	74	26
Sodium chloride, 2 *N*......	0.46	12.9	14.0	5.07	72	28
Sodium chloride, 2 *N*.......	0.36	10.1	9.0	3.26	76	24
	0.56	15.7	28.0	10.14	61	39

chlorohydrin actually produced in the experiment, are expressed in terms of normality factor.

Fig. 1 shows more graphically the influence exerted by the various factors upon the ratio of ethylene consumed in chlorohydrin formation to that consumed in ethylene chloride formation.

It is not safe to draw decided conclusions from so few experiments, but the above results, as far as they go, seem to indicate: (1) hydrochloric acid, by itself, even when in concentration 2 *N*, does not hinder the conversion of ethylene exclusively into chlorohydrin. But when the concentration of the latter has reached about 3 % (HCl = 2.3 *N*) ethylene chloride commences to be produced in considerable amounts (2) Chlorohydrin, by itself, even in *N* concentration, has no bad influence upon chlorohydrin formation On the contrary, the presence of some chlorohydrin in the solution at the beginning of the operation, seems to increase the speed of the absorption of ethylene. When, however, in the course of the reaction the concentration on chlorohydrin becomes about 2 *N*, [the acid at the same time becoming about *N*, ethylene chloride commences to form. (3) The combined effect of chlorohydrin and acid is of far greater influence than the individual influence of each would lead one to expect. A *N* concentration of each, when simultaneously present, favors the formation of ethylene chloride. (4) Neutralization of hydrochloric acid during the course of the reaction would appear to be harmful rather than beneficial. The salts thus produced show a more deleterious effect than the acid in chlorohydrin formation. Neutralization by calcium or magnesium hydroxide is likely to prove less harmful than by sodium hydroxide.

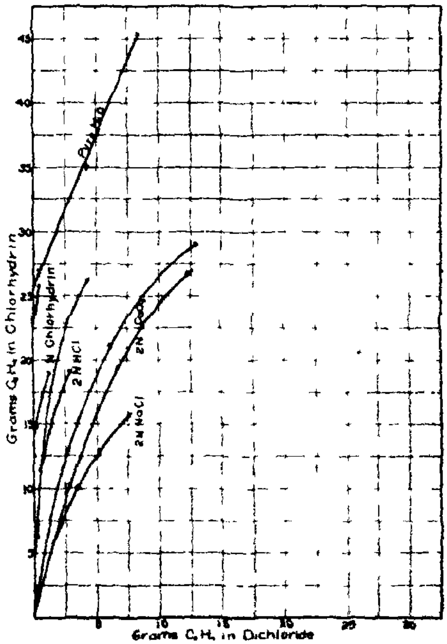

Fig 1.—Curves showing effects of acids, salts, etc., on the formation of CH_2OHCH_2Cl and $C_2H_4Cl_2$.

The additional small amount of free acid, simultaneously produced with the chlorohydrin in the course of the tests with the salts, is not taken into account.

Thus, it would seem, that for practical purposes it is not advisable to go beyond 7 or 8% of chlorohydrin concentration, although very good stirring may raise this somewhat. It also seems best not to neutralize the acid while the reaction is progressing, unless this becomes desirable in order to prevent corrosion of the apparatus.

Fractional Distillation of Chlorohydrin Solutions.— Pure chlorohydrin is described in the literature as possessing a boiling point between 128° and 132°. In our experience, chlorohydrin, known from its analysis to be pure, boils at 128° to 128.5°, under 730–735 mm. pressure. Although the difference in the boiling points of chlorohydrin and water is greater than that of water and alcohol, yet in the past the separation of chlorohydrin from water by fractional distillation was not attempted, for the reason, presumably, that chlorohydrin was believed to distil all with the water. Carius' early observation[1] that chlorohydrin distils over with the first portions of the water, has apparently never been utilized by subsequent workers. That statement is correct only when the concentration of chlorohydrin is within certain limits, as will be shown below. We, too, found that with 10 to 15% solutions of chlorohydrin, the hydrin distils over almost wholly with the first half of the water, the thermometer usually indicating 98° to 99°. But when the distillate was collected in small fractions and these were examined with the refractometer, we found that the first fractions were richest in chlorohydrin, the strength rapidly dropping off as the distillation proceeded. From a series of experiments it was determined that chlorohydrin and water, in the proportion of 42.5% of the former and 57.5% of the latter, make a constant boiling mixture which boils at 95.8° under 735 mm. (Fig. 2). Consequently, when a solution richer than the constant-boiling mixture is distilled, the latter comes over first, and almost pure chlorohydrin towards the last (Fig. 3, 50% Solution). On the other hand with solutions poor in chlorohydrin content, the very first fractions on distillation will tend to approach in their composition the constant boiling mixture, and will consequently be the richest. This was verified on concentrations of 5, 10 and 15% of

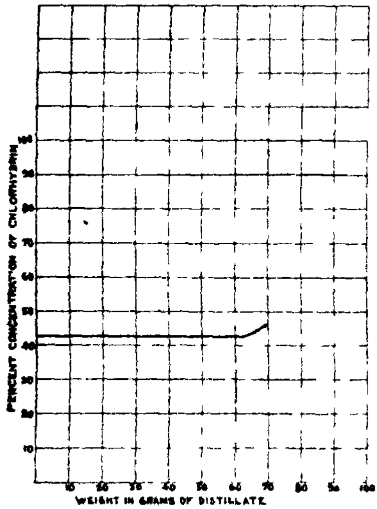

Fig. 2.—Constant-boiling mixture
Original concentration, 43.7%

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[1] *Ann.*, **126**, 198 (1863).

chlorohydrin, respectively (Fig. 4). It is apparent that the more dilute the solution is, the greater, relatively, is its tendency to enrich itself in the first fractions on distillation. By the time $^1/_2$ of the total original solution had distilled, it carried over 80%, and more, of all the chlorohydrin, and the concentration in this distillate was now almost double that of the original solution.

It should be mentioned that J. C. Irvine[1] arrived at similar conclusions, based upon similar findings. He, too, employed the refractometer in the course of distillation of aqueous solutions of chlorohydrin.

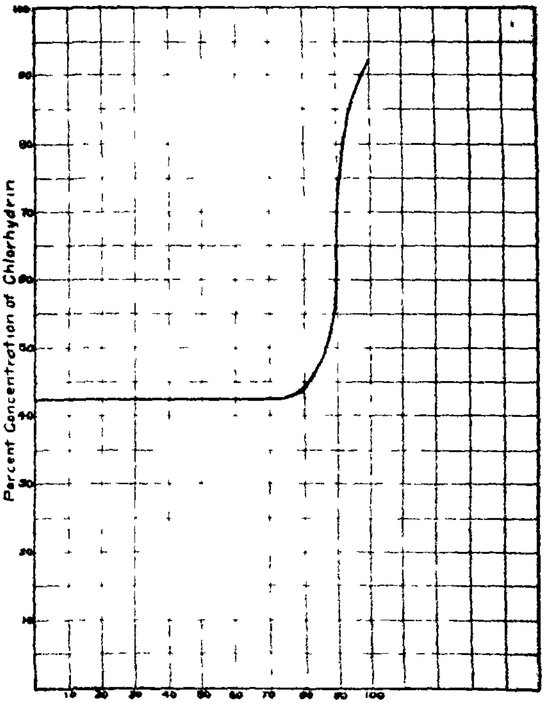

Fig. 3.—Curve for 50% solution.

Effect of Hydrochloric Acid and of Salts upon the Course of the Distillation.—When chlorohydrin is prepared as described, there is produced as a by-product an equivalent amount of hydrochloric acid, or, if progressively neutralized, an equivalent amount of some salt. The separation of chlorohydrin from the acid solution can be accomplished through fractional distillation just as readily as from a neutral solution, and neutralization of the acid is not necessary unless it be desirable to avoid the corrosive action of the acid upon the distillation vessel.

The refractive indices of dil. hydrochloric acid solutions are almost identical with those of chlorohydrin when of the same molecular concentrations. Also, the refractive index of a mixture consisting of acid and chlorohydrin is an additive quantity, as we found by experiment. Consequently, by determining in the course of a fractional distillation the refractive indices of the fractions on the one hand, and by titration the acid content on the other hand, one may follow the progress of separation of chlorohydrin from acid by distillation. In the following experiment 25 cc. of 2 *N* chlorohydrin solution was mixed with 25 cc. of 2 *N* hydrochloric acid, the resulting mixture approximating what is usually obtained in actual practice, *i. e.*, a solution containing about 8% of chlorohydrin. The mixture was distilled, using an ordinary fractionating column with 3 bulbs, and the distillate was collected in 9 fractions.

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[1] Report at the Bureau of Mines.

TABLE II

Fraction	Weight G	Refr index	Acid Cc 0.1 *N*	Acid Combined % of total	Chlorohydrin G	Chlorohydrin Concentration in %	Chlorohydrin Combined % of total
1......	5.9	1.361	0.00		1.52	25.7	40.3
2. .	8.1	1.3486	0.03		1.16	14.3	71.1
3. . ..	5.1	1.343	0.03		0.47	9.2	83.5
4 ..	6.0	1.339	0.00		0.33	5.5	92.3
5. ..	5.0	1.337	0.00		0.185	3.7	97.3
6 ...	5.0	1.335	0.03		0.05	1.0	98.4
7. ..	5.0	1.337	3.8	3.3	0.05	1.0	100.0
8.	5.1	1.373	57.8	51.4			
9.	2.8	1.3776	31.2	80.1			

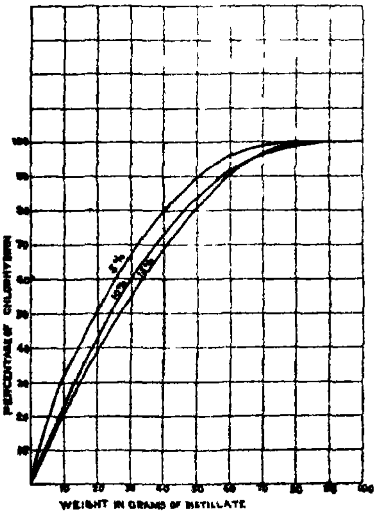

Fig. 4.—Superimposed curve of 5%, 10%, 15% solutions

Fig. 5 shows in a very striking manner how readily and completely chlorohydrin may be distilled from the dil. hydrochloric acid solution, leaving all the acid behind

As to the effect of salts, experiments have shown that a solution containing 5% of chlorohydrin and only an equivalent amount of sodium or calcium chloride is but slightly affected by the presence of the latter. But in a 10% solution the influence becomes apparent after the first $^1/_{10}$ of the solution has distilled over, and is quite appreciable after the first $^1/_5$ has gone over. Again, if such a solution is saturated with calcium chloride, the first fraction of the distillate, which is equal in volume only to $^1/_3$ of the original solution, contains 95% of all the chlorohydrin originally present. In other words, the 10% solution becomes now a 30% solution of chlorohydrin with practically no loss of the product. These facts are shown in Fig. 6.

It is not possible to get as concentrated distillates by saturating dilute solutions of chlorohydrin with salt as when saturating with calcium chlo-

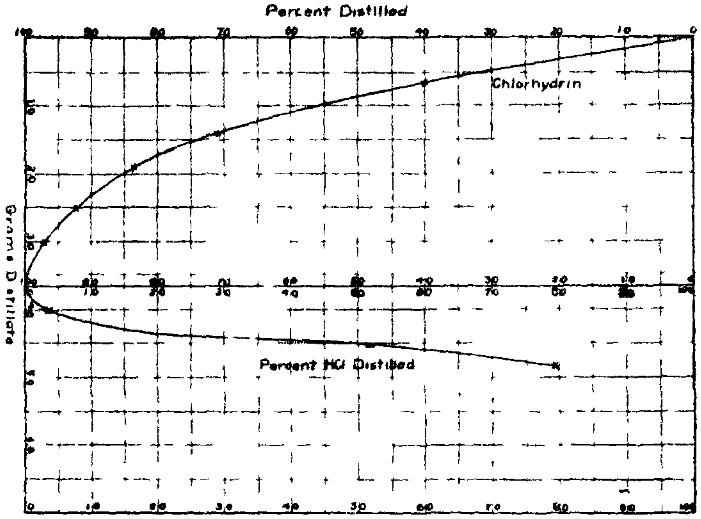

Fig 5.—Curve for fractionation of equivalent parts of chlorohydrin and HCl in H_2O.

ride, due to the great difference in the solubility of the two chlorides. The following examples show what can be accomplished by a successive combination of the salts. About 8 liters of water was treated with ethylene and chlorine until a 7.3% concentration of chlorohydrin was produced. This mixture, 9 liters, was neutralized with lime and distilled until 4 liters was collected. The distillate was now saturated with salt and again distilled and 1600 cc collected. This distillate was now saturated in the cold with commercial calcium chloride, and distilled until one liter was collected. The strength of the final solution was 64% of chlorohydrin. Thus, by three distillations, all the chlorohydrin originally present in 9 liters, was concentrated into one, with practically no loss of the product.

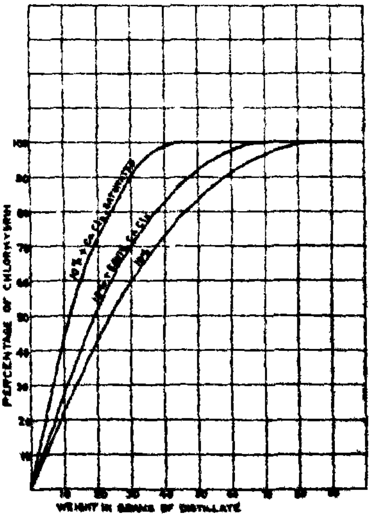

Fig 6.—Superimposed curves of 10% solutions, one containing an equivalent quantity of $CaCl_2$, and one saturated with $CaCl_2$.

Salting Out the Chlorohydrin.—Carius, in describing the properties of chlorohydrin, makes the statement that chlorohydrin readily separates on the addition of soluble salts to its aqueous solution. The statement is misleading, and this may account for the fact that, subsequently, this property has not been utilized for the separation of chlorohydrin. The nature of the salt, the concentration of the chlorohydrin, the temperature of the solution,—each of these constitute a very important factor in this operation. Thus, with sodium chloride, very little, if any, chlorohydrin is thrown out of a solution, unless more than 16 to 18% is present, for water saturated at room temperature simultaneously with both salt and chlorohydrin, retains 16 to 17 g. of the latter per 100 cc. of liquid. By raising the temperature, more salt will be dissolved, but on the other hand, the solubility of chlorohydrin in water increases also to such an extent that no chlorohydrin is separated even from a 50% solution. If now such a solution is allowed to cool down slowly to room temperature, an oil rich in chlorohydrin will appear on the top. It is evident, therefore, that it would hardly be advisable to resort to salting out chlorohydrin with ordinary salt, unless the solution contains 30 to 35% of the hydrin. Under such circumstances, about $^1/_2$ of the total separates as an oil on the surface; its composition is about 30% water, 70% chlorohydrin, and it carries 7.2 g. sodium chloride per 100 cc. of oil.

Sodium sulfate gives far more satisfactory results than sodium chloride. Saturation with the sulfate at ordinary room temperature has very little effect, but at slightly higher temperatures, 32 to 33°, a great deal more of the sulfate goes into solution. The separation of the oil commences when the solution contains 7 g. of the sulfate per 100 cc., and the amount of oil continues to increase until the aqueous solution is saturated, at that temperature, with the sulfate, containing 25 g. of it per 100 cc. The aqueous solution is now only about 7% chlorohydrin, while the composition of the oil is about 68% chlorohydrin and 32% water, and it carries only about 0.65 g. of sodium sulfate per 100 cc of oil. Obviously, sodium sulfate at 32 to 33° is decidedly a more suitable salting out agent than sodium chloride at room temperature.

The following procedure may be employed when working on a laboratory scale: After all the chlorohydrin has separated on saturating the solution at 32° with sodium sulfate, the mixture is cooled down without disturbing the liquids. If now a crystal of the salt is dropped in, crystallization in the supersaturated aqueous solution ensues at the point of juncture of the two liquids. So dense is the mass of crystals at the juncture that the oil can be decanted readily, free from contamination with the lower layer.

A combination of the two salts may be employed with advantage. Stopping slightly short of saturation with sodium chloride, and then finishing with just a small amount of sodium sulfate, all at room temperature, a satisfactory separation may be had, the aqueous solution being only 10% strong in chlorohydrin.

Magnesium sulfate, ammonium sulfate, aluminum sulfate, were found to induce separation; magnesium chloride and calcium chloride, on the other hand, proved ineffective. The subject of salting out deserves very careful attention, and more work, of greater accuracy, needs to be done in this connection.

In addition to distillation and salting out, we still have the old standard method of extraction with immiscible solvents. On a technical scale, benzene would offer decided advantages over ether, which has been used generally in the past for the extraction of chlorohydrin from its aqueous solutions. Ethylene chloride, the by-product in the manufacture of chlorohydrin, could also be employed for this purpose.

It is obvious that the isolation of chlorohydrin from its dilute aqueous solution, can be accomplished advantageously by a judicious combination of all three methods,—distillation, salting out and extraction with immiscible solvents in a continuous extraction apparatus.

Hydrolysis of Chlorohydrin.—The hydrin is very slowly hydrolyzed during the distillation of its dilute solution in water. The following data give some idea of this loss through hydrolysis. A solution of chlorohydrin, 2.706 *N* (21.6%), was boiled under a reflux condenser, and the acid produced was estimated from time to time.

TABLE III.

Time, hours	Acid concentration, *N*	% hydrolyzed
0	0.0164	0.0
1	0.0452	1.06
2	0.0822	2.43
5	0.1946	6.60
10	0.3330	12.30
16	0.441	16.30

2. β,β-Dichloroethylsulfide.

The conversion of the hydrin into dichloroethylsulfide involves only two steps and the employment of the very simple, readily accessible materials, namely, sodium sulfide and hydrochloric acid.

Thiodiglycol.—We found that it was unnecessary to employ such a large excess of sodium sulfide as was recommended by V. Meyer and by H. T. Clarke in order to convert chlorohydrin into ethyl sulfide.

$$2HOC_2H_4Cl + Na_2S = HO.CH_2CH_2.S - CH_2CH_2OH + 2NaCl.$$

Instead of 4 mols. of the sulfide, 1.5 mol., and less, was found to be not only sufficient, but preferable, in that a purer product resulted. Another point of significance, in considering the technical possibilities of the process, is the fact that for good yields it is not essential to employ very concentrated solutions of chlorohydrin; 20% solutions gave results as good as the 80 or 100% solutions. Large scale operations alone could have decided whether it be preferable to get rid of the water before conversion of the chlorohydrin into thiodiglycol or after its conversion, but at the one or the other stage that would have to be done. Of course, less evaporation is entailed in obtaining concentrated solutions of chlorohydrin than would be required in obtaining equivalent concentrations of thiodiglycol. On a laboratory scale it was found convenient to employ 40 to 80% chlorohydrin solutions. The weighed amount of the solid sodium sulfide containing water of crystallization is added directly to the chlorohydrin solution, and the reaction is completed by heating the mixture for a short time. The solution is now neutralized, sulfuric acid being preferable to hydrochloric in that it introduces no additional amount of water, and the water evaporated, reduced pressure being safely used as the glycol is not volatile. The residual salts are impregnated with the syrupy oil of the glycol, and the next problem is to separate the glycol from the salts. On a large scale p obably centrifuging, followed by washing with a little alcohol, would prove serviceable. In the laboratory, the glycol can be extracted with alcohol, and is obtained pure on the evaporation of the solvent.

The yield of the glycol is very satisfactory, being easily 90 to 95% of the calculated amount, and frequently even better than that. It is a thick, syrup, non-volatile even at 200°, non-distillable under reduced pressure without decomposition. It is immiscible with most of the organic solvents, but is soluble in chloroform The only certain way of determining the purity of a technical sample of glycol is to determine how much mustard gas it yields. An attempt was made to prepare the glycol pure by extracting its aqueous solution with chloroform. But on drying this with calcium chloride it was found that nearly all the glycol had combined with the salt. It behaves in this respect like the ordinary alcohols.

Dichloroethylsulfide.—The usual methods of replacing alcohol hydroxyl groups by chlorine can be applied to this problem, but the simplest procedure is to heat the thiodiglycol with conc. hydrochloric solution.[1] With this procedure in view it becomes unnecessary to isolate the thiodiglycol as such, and the two steps, the preparation of the glycol and the dichloride, can then readily be combined into one operation. To the solid sodium sulfide containing water of crystallization the required amount of 70 to 80% chlorohydrin is added. The solution process of the sulfide is endothermic, the reaction with chlorohydrin is exothermic, and the two just about balance each other. When the reaction is over, the excess of sodium sulfide is neutralized with 90% sulfuric acid. To this, *without previous evaporation*, concentrated hydrochloric acid is added, and the precipitated sodium salts are filtered off by suction and washed with more acid. On warming the clear, yellow hydrochloric acid solution of the glycol to 60–75°, the dichloroethylsulfide separates as a heavy, yellow oil. The acid solution is separated and can be used again after being fortified with hydrogen chloride. The oil is washed with water, and after filtering through a layer of calcium chloride or sodium chloride, it is sufficiently pure for all purposes, unless a C. P. article is desired. We have repeatedly obtained yields from 90 to 98%, based upon the amount of chlorohydrin taken for the experiment.

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[1] H. T. Clarke, *Loc. cit.*

The undistilled material retains very little moisture and hardly any hydrochloric acid. In fact, passing hydrogen chloride into pure mustard gas, the latter takes up, under the most favorable conditions, not more than 1.5% of its weight, and this can be swept out readily with a little dry air.

If further purification is desired, distillation under reduced pressure gives the best results. A slight decomposition occurs when the product is subjected to prolonged heating, as when distilling large amounts of the material. The distilled and pure product is absolutely colorless, and remains colorless on long exposure to light. A sample which has been exposed for almost a year shows no trace of coloration.

The dichloride is readily hydrolyzed by alkalies, silver nitrate solution, and even to a slight extent with cold water. Consequently, the reaction between the diglycol and hydrochloric acid is a reversible one.

$$(HOC_2H_4)_2S + 2HCl \rightleftarrows (ClC_2H_4)_2S + H_2O.$$

It was found that the conversion of the glycol into the dichloride is done best at 65–75°, and that at the end of the operation the supernatant acid solution at 70° should still remain saturated with hydrochloric acid, *i. e.*, it should contain 33% of acid. Under such conditions, one drop of pure glycol gives, with 25 cc. acid, a fairly visible amount of mustard gas. With a concentration of acid of 30%, even two drops fail to give any dichloride; with 25% several tenths of a cubic centimeter are required, while with acid 20% strong, even 2 cc. do not produce turbidity. It may be mentioned that the above equilibrium between acid and glycol is not readily established when starting from the other end, *i. e.*, hydrolyzing mustard gas with solutions of hydrochloric acid of various strengths. For instance, 0.5 cc. of mustard gas was heated at 70° with 15 cc. of 20% hydrochloric acid for a week, with frequent stirring,—but not more than half of the oil disappeared. Apparently the hydrolysis of the dichloride must proceed at a much slower rate than the formation of the dichloride from the glycol.

To summarize, with the problem of producing ethylene on a scale hitherto unattempted, solved in a satisfactory manner[1] and with the conditions for the successful manufacture of chlorohydrin determined, the foundation of a process for producing mustard gas on a technical scale was assured. Another process, however, namely, the one based upon the sulfur chloride reaction, was ultimately adopted in this country.

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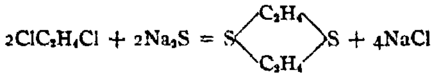
[1] Dorsey, *J. Ind. Eng. Chem.*, 11, 286 (1919).

3. Action of Sodium Sulfide on Ethylene Chloride.

The possibility of making mustard gas from ethylene chloride according to the equation,

$$2\mathrm{Cl_2C_2H_4Cl} + \mathrm{Na_2S} = (\mathrm{ClC_2H_4})_2\mathrm{S} + 2\mathrm{NaCl}$$

has been studied, but the results were negative. The reaction was found to proceed further than desired, even when at room temperature.



$$2\mathrm{ClC_2H_4Cl} + 2\mathrm{Na_2S} = \mathrm{S}\begin{matrix}\diagup\mathrm{C_2H_4}\diagdown \\ \diagdown\mathrm{C_2H_4}\diagup\end{matrix}\mathrm{S} + 4\mathrm{NaCl}$$

The ill-smelling, but non-toxic, crystalline disulfide was produced, or one of its two polymers,[1] in either case only comparatively small amounts being formed, from 1 to 5% of the theoretical amount. Ethylene bromide gave the same product, but in larger yields With the object in view to keep down the mass of the reacting metal sulfide, attention was turned to the use of insoluble sulfides, such, however, as possess the tendency to form soluble chlorides. Zinc sulfide, ferrous sulfide, etc., were tried, but they gave no better results.

General considerations concerning the reactivity of halogen derivatives of this group of compounds suggest that the dichloroethylsulfide is likely to prove more reactive than ethylene dichloride. Compare ethyl chloride with ethylene dichloride, and we notice the stabilizing effect of the second halogen. On the other hand, compare ethyl chloride with glycol chlorohydrin and we notice, if anything, the opposite effect of the oxygen atom. Now, in mustard gas the sulfur atom is with respect to the halogen in the same position as the oxygen in chlorohydrin, and we may expect a similar influence by sulfur as by oxygen. Experiments with pure mustard gas gave results which were quite decisive: sodium sulfide converts dichloroethylsulfide *very readily* into the disulfide. In the following experiments one cc. (1.3 g.) of mustard gas was taken in each case, mixed with sodium sulfide and allowed to stand at room temperature. Curiously enough, the more dilute the solution of sodium sulfide employed in the experiment, the quicker did the reaction set in, and the larger the final yield of the disulfide in a given time. This difference in action may be due to the greater alkalinity of the conc. sodium sulfide solutions, and the consequent more extensive hydrolysis of the dichloride. With the dilute solution, the precipitation of the disulfide begins in about an hour, when cold, and much quicker when heated.

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[1] V. Meyer, *Loc. cit*

	Strength of sodium sulfide solution.	Days standing.	Yield in g.	Calc. yield, g.
I.	20%	5	1.10	1.30
II.	30%	8	0.72	1.30
III.	50%	10	0.45	1.30

The greater velocity of reaction toward sodium sulfide possessed by dichloroethylsulfide than by ethylene dichloride precluded the possibility of obtaining mustard gas by this reaction, and the work in this direction was not pursued further.

4. Summary.

1. It has been shown that ethylene chlorohydrin can readily be prepared from ethylene and chlorine in presence of water, at comparatively low temperatures, 0–20°. It was found unnecessary, and apparently undesirable, to keep down, through neutralization, the amount of hydrochloric acid which is being produced in the course of this reaction.

2. Concentrations as high as 15% of chlorohydrin have been obtained, but it was found not advisable to go beyond 8%, on account of the proportionately increasing amounts of ethylene chloride produced at the expense of chlorohydrin. Some factors which affect adversely the yield of chlorohydrin were determined and they can be arranged in order of their increasing influence: chlorohydrin, hydrochloric acid, magnesium chloride, calcium chloride, sodium chloride; also deficient stirring.

3. It has been found that chlorohydrin and water, 42.5% of the one and and 57.5% of the other, make a constant boiling mixture, 95.8°. In virtue of this property, it has been shown, dilute solutions of chlorohydrin can be readily enriched by distillation, especially when salt or calcium chloride is added to the solutions to be distilled. From the concentrated solutions pure chlorohydrin, b. p. 128°, can be obtained.

4. Methods for salting out chlorohydrin from its aqueous solutions have been described, and it is shown that about 70% strong solutions can be obtained in this manner. By combining the 3 processes, distillation, salting out and extraction with immiscible solvent, chlorohydrin can be readily obtained pure.

5. The conditions have been determined which permit an almost quantitative conversion of chlorohydrin into mustard gas, starting with either dilute or concentrated aqueous solutions of chlorohydrin.

6. It was found impossible to get mustard gas by the action of metal sulfide upon ethylene chloride. The reason therefore was found to lie in the much greater reactivity towards these metal sulfides possessed by the mustard gas itself than by ethylene chloride.

To Mr. F. W. Sullivan, Jr., and Mr. F. H. Kranz the writer wishes to express his great obligation for their able assistance in the course of the work described in this paper.

ANN ARBOR, MICH.

[Contribution from the New York Sugar Trade Laboratory, Inc.]

THE COMPOSITION AND CALORIFIC VALUE OF SIRUPS AND MOLASSES DERIVED FROM SUGAR CANE.

By C. A. Browne.

Received June 25, 1919

Very accurate data are available as to the calorific value of the sucrose and invert sugar in sirups, but very little information is obtainable regarding the actual combustion units of the organic non-sugars which make up usually from 4 to 18% of the dry substance in the sirups and molasses derived from the sugar cane. It was to gain more knowledge upon the latter subject that the present investigation was begun.

Changes in Constituents of Juice during Sirup Manufacture.

The organic non-sugars in the sirups and molasses derived from the sugar cane consist partly of products derived from the juice of the sugar cane and partly of decomposition products formed during manufacture. In order to arrive at some understanding of the nature of these substances a brief reference must be made to the changes produced in the constituents of cane juice by the processes of clarification, filtration and evaporation.

In Table I a comparison is given of the approximate composition[1] of sugar cane juice and of low grade cane molasses.

Table I.—Composition of Sugar Cane Juice and Molasses.

	Juice. %	Molasses %
Water	83.00	20.00
Sucrose	15.00	30.00
Invert sugar	0.80	30.00
Ash	0.45	8.00
Proteins	0.05	..
Nucleins	0.03	.
Proteoses	0.01	0.10
Nitrogenous bases (guanine, etc.)	Trace	0.40
Amids (asparagine, glutamine, etc.)	0.05	0.50
Amino acids (aspartic, etc.)	0.12	1.50
Other organic acids (aconitic, etc.)	0.10	1.50
Gums and pectins	0.10	2.00
Fiber particles	0.12	..
Fat and wax	0.10	..
Earthy matter	0.06	..
Chlorophyll, etc.	0.01	..
Decomposition products { lactic acid, saccharinic acid, glycinic acid,[2] caramel, etc.	..	6.00
	100.00	100.00

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[1] According to results given in *Bull.* 91 (1907) of the Louisiana Sugar Experiment Station.

[2] The term "glycinic" or "glucinic acid" was first introduced by Peligot to describe one of the unstable acid decomposition products formed by heating glucose with alkalies. See Lippmann's *Chemie der Zuckerarten*, 1, 330–1.

In the clarifying operations of liming, heating and filtering a considerable change is effected in the composition and distribution of the juice ingredients. The suspended impurities, removed from the cane in milling, such as fiber particles, fat and wax, dirt, chlorophyll, etc., are precipitated, the proteins and nucleins are coagulated, and a part of the gums and ash constituents are removed. But with the elimination of these ingredients a new class of degradation and decomposition products enters into solution. By the action of lime and heat a part of the nucleins are decomposed into nitrogenous bases, or purins, and variable amounts of the reducing sugars are destroyed with the formation of soluble salts of lactic, saccharinic, glycinic and other acids. A certain amount of sucrose also undergoes dehydration with the formation of caramel. The extent of these changes will vary with conditions. When an excess of lime is used the formation of new substances by the decomposition of nitrogenous ingredients and reducing sugars may proceed to such an extent that their presence affects the flavor of the product, the sirup, or molasses, being then, as is said, lime-burnt.

The effect of the above-mentioned changes is shown most strikingly by comparing the compositions of the ash of cane juice and cane molasses. Table II gives the average distribution of some of the constituents in the ash of cane juice and cane molasses, according to analyses made in Louisiana.[1]

TABLE II.—COMPOSITIONS OF ASH OF SUGAR CANE JUICE AND MOLASSES.

Ingredient, as oxide.	Juice %.	Molasses. %.
Potassium (K_2O)	45.54	50.83
Sodium (Na_2O)	0.44	0.78
Calcium (CaO)	4.01	7.09
Iron (Fe_2O_3)	0.95	0.32
Aluminum (Al_2O_3)	0.54	0.24
Silica (SiO_2)	6.55	3.91
Phosphates (P_2O_5)	5.72	2.64
Sulfates (SO_3)	21.78	9.91
Carbonates (CO_2)	3.55	11.88
Alkalinity of ash (cc. 0.1 *N* acid to neutralize 1 g. of ash)	28	94

While the above results do not represent juice and molasses of the same origin, the analyses are an average of the product from different kinds of cane and from different factories. They may be considered therefore as fairly typical.

A comparison of the analyses shows about 17% less silica, phosphoric acid and sulfuric acid and about 17% more potash, soda, lime and carbonic acid in the ash of the molasses. These results, when considered in connection with the increase in alkalinity of the ash, show that a part of the basic elements of the mineral salts in cane juice enter as a result of clarification into new organic combinations with acid decomposition products, such as lactic, saccharinic and glycinic acids. In the process of evaporating and boiling the glycinic acid undergoes a partial dehydration with formation of humic acid substances of higher carbon content.

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[1] Louisiana Sugar Expt. Sta., *Bull.* 91 (1907).

In the manufacture of what is termed "Refiner's Sirup" a part of the non-sugars in cane molasses are removed in the blow-ups and char filters. There is a further decrease in the mineral sulfates and phosphates and also in the calcium salts of organic acids. The decrease in glycinic acid and its decomposition products is made most apparent by the removal of color.

Changes in Calorific Value of Juice during Sirup Manufacture.

The calorific values of some of the constituents which may occur in the sirups and molasses derived from the sugar cane are given by various authorities as follows:

Formula.	Calories[1] per g
Aconitic acid, $C_6H_6O_6$	2.750
Aspartic acid, $C_4H_7NO_4$	2 900
Asparagine, $C_4H_8N_2O_3$	3 444
Lactic acid, $C_3H_6O_3$	3.666
Invert sugar, $C_6H_{12}O_6$	3 750
Sucrose, $C_{12}H_{22}O_{11}$	3.955
Saccharin, $C_6H_{10}O_5$.	4 055
Gums, estimated for $(C_6H_{10}O_5)n$	4 100
Humic acid, $C_{18}H_{14}O_6$	5.880

As regards the calorific values of the decomposition products formed during sirup manufacture, we may make a triple classification. (1) Little or no change in calorific value, as in the formation of lactic acid ($C_3H_6O_3$) and saccharinic acid ($C_6H_{12}O_6$) from invert sugar. (2) A decrease in calorific value, as in the formation of invert sugar from sucrose. (3) An increase in calorific value, as in the formation of dehydration products such as caramel, saccharin, glycinic acid and its humoid derivatives.

In the manufacture of sirup, the inversion of sucrose produced by concentrating sugar cane juice in acid solution, would tend, therefore, to diminish the heat units of the organic solids, while the formation of dehydration products by concentrating this juice in alkaline solution would tend to increase the heat units of these solids. As regards the organic non-sugars alone the operations of the sirup house and sugar factory would tend on theoretical grounds to cause an increase in their calorific value. On the other hand, the filtration of cane molasses over bone black might produce a variable result according to the selective action of the char upon the non-sugars of lower calorific value, such as aconitic and aspartic acids, and upon those of higher calorific value such as glycinic acid and its dehydration products. The latter being in excess in ordinary cane molasses, filtration over animal charcoal would tend to eliminate more salts of glycinic acid than of aspartic or aconitic acid. These general deductions have been in large part confirmed by the following practical tests.

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[1] The calorie used in this paper is the greater or kilogram calorie, *i e.*, the amount of heat required to raise the temperature of one kilogram of water one degree centigrade.

Experimental Part.

The following 8 samples were selected for comparison as to composition and calorific value:

1. A sample of the clear mother liquor from pure concentrated sugar cane juice. The cane juice was concentrated by simple evaporation, without the addition of lime or other chemicals, by Dr. F. W. Zerban at the Louisiana Sugar Experiment Station. After as much of the sucrose as possible had been crystallized from the sirup, the mother liquor was removed by decanting and filtering.

2. A sample of open-kettle molasses manufactured by Aurelien Simoneaux at Church Plantation, Plattenville, La. The expressed cane juice was treated with sulfur dioxide, limed, heated, allowed to settle and the clear juice concentrated in an open kettle heated by steam coils. The massecuite, after crystallizing in a cooler, was drained in hogsheads; the drippings constituted the molasses, from which the sample was taken

3. A sample of first Cuban molasses, supplied by Dr G. L. Spencer from Central Tinguaro, Cuba. The juice, from which the molasses came, was clarified with lime by the ordinary defecation process.

4. A sample of Refiners Sirup made by the Franklin Sugar Refining Company in Philadelphia, Pa.

5. A sample of Refiners Sirup made by the American Sugar Refining Company in Boston, Mass.

6. A sample of Refiners Sirup made by the American Sugar Refining Company in Jersey City, N. J.

7. A sample of Refiners Sirup made by the National Sugar Refining Company in Yonkers, N. Y.

8. A sample of Refiners low grade Molasses (black strap) made by the National Sugar Refining Company in Yonkers, N. Y.

TABLE III.

Analyses of the 8 Samples of Sirups and Molasses.

Sample	1	2.	3.	4.	5.	6.	7.	8.
Water	29.64	28.16	24.91	17.85	16.77	17.30	18.51	19.60
Invert sugar	13.93	14.28	12.84	29.72	33.18	31.19	26.76	22.53
Sucrose	49.86	51.92	48.13	36.12	38.00	37.57	41.58	37.87
Ash	3.60	2.50	4.82	5.30	4.46	5.97	4.04	6.53
Undetermined organic matter	2.97	3.14	9.30	11.01	7.59	7.97	9.11	13.47
Total	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
Alkalinity of ash, cc. 0.1 *N* acid to neutralize 1 g. of ash	51.2	92.9	64.2	81.5	77.0	102.2	123.4	126.2

In the above analyses water was determined by evaporating about 2 g. of the carefully weighed product in a glass-stoppered weighing bottle in a vacuum oven at a temperature not exceeding 70°. The drying was continued until constancy in weight was secured. The vacuum caused the substance to foam up in drying and the residue consisted of a porous, friable, hygroscopic mass. It was sealed and set aside for determination of the Calories.

Invert sugar was determined by the customary gravimetric method of copper reduction

Sucrose was determined by the Clerget method of double polarization and also from the increase in copper reducing power after inversion. The average of the results by the two methods was the value taken

Ash was determined by first carbonizing the product in a platinum dish at low heat. The residue was then ground and extracted with distilled water on an ashless filter. The carbonaceous residue was then incinerated in the platinum dish until a white ash was obtained, the aqueous extract of soluble ash was then added, the whole evaporated to dryness, heated to dull redness, cooled and weighed The alkalinity of the ash was determined in the usual way by titrating with 0 1 *N* sulfuric acid.

Since the determinations of Calories were made upon the dry solids, the results of Table III were recalculated to a moisture-free basis

TABLE IV

Percentages Calculated to a Moisture-free Basis

Sample	1	2	3	4	5	6	7	8
Invert sugar	19 80	19 88	17 10	36 18	39 86	37 71	32 84	28 02
Sucrose	70 86	72 27	64 10	43 97	45 66	45 43	51 02	47 10
Ash	5 12	3 48	6 42	6 45	5 36	7 22	4 96	8 12
Undetermined organic matter	4 22	4 37	12 38	13 40	9 12	9 64	11 18	16 76
Total	100 00	100 00	100 00	100 00	100 00	100 00	100 00	100 00

Determinations of the Calories per gram of the moisture-free solids in the above 8 samples were performed by J. A. Fries of the Pennsylvania State College, with the following results·

Sample	1	2	3	4	5	6	7	8.
Calories per g of solids	3 661	3 765	3 726	3 640	3 675	3 600	3 715	3 685

The results show that the dry matter of sirups and molasses derived from the sugar cane has a heat value ranging from 3 6 to 3.8 Calories per g.

The calorific equivalents of the invert sugar and sucrose in the moisture-free solids of the 8 samples, as calculated from the results of Table IV are as follows·

Sample	1	2	3	4	5	6	7	8
Invert sugar.	0 743	0 746	0 641	1 357	1 495	1 414	1.232	1 051
Sucrose, ...	2 803	2 858	2 535	1 739	1.805	1 797	2 018	1 863
Cals. of sugars per g. of solids . .	3 546	3.604	3.176	3.096	3 300	3 211	3.250	2.914

The Calories due to the undetermined organic matter, found by subtracting the Calories of the sugars from the total Calories per g. of solids, are as follows:

Sample.	1.	2.	3.	4.	5.	6.	7.	8.
Cals. of undetermined organic matter per g. of solids	0.115	0 161	0.550	0.544	0 375	0.389	0.465	0.771

From the above figures and the percentages of undetermined organic matter in Table IV, the Calories per g. of undetermined organic matter were computed to be as follows:

Sample	1.	2.	3.	4.	5.	6.	7.	8.
Cals per g. of undetermined organic matter	2 725	3.684	4 443	4 060	4 112	4 035	4 159	4.600

The calorific value of the undetermined organic matter in the various products is lowest in sugar cane juice (Sample 1) and highest in the residual molasses (Samples 3 and 8). In the open kettle molasses (Sample 2), made by acid clarification with sulfur dioxide, the destructive action of lime is less apparent than in those products where lime had been used in greater excess. Comparing the sirups which had passed over bone black (Samples 4, 5, 6 and 7), with the two residual molasses the removal of dehydration products is indicated not only by the lighter color but by the lower calorific value of the organic non-sugars.

The calorific values of the undetermined organic matter, as above calculated, are no doubt a little too low in all cases, owing to the retention of water of crystallization by some of the organic and inorganic constituents in drying at 70°. Such a retention would not only lower the Calories of the solids but would make the percentages of undetermined organic matter too high. Unfortunately, no means could be found for estimating the water of crystallization retained by the vacuum-dried solids of sirups and molasses, as elevating the temperature much above 70° caused some of the organic matter to decompose. As an additional check, therefore, upon the accuracy of the work a comparison of 6 of the samples was made upon the basis of carbon content.

The carbon content of the organic constituents of the sirups derived from the sugar cane varies from about 36% in the case of aspartic acid to 60% or more in the case of humoid decomposition products. The following is a classification of some of these constituents:

Formula.	Carbon. %
Aspartic acid, $C_4H_7NO_4$	36 10
Asparagine, $C_4H_8N_2O_3$	36.36
Invert sugar, $C_6H_{12}O_6$	40.00
Aconitic acid, $C_6H_6O_6$	41.38
Sucrose, $C_{12}H_{22}O_{11}$	42.10
Gums, $(C_6H_{10}O_5)n$	44.44
Glycinic acid, $C_{12}H_{18}O_9$	47.06
Caramelan, $C_{12}H_{18}O_9$	47.06
Humic acid, $C_{18}H_{14}O_6$	66.26

If the conclusions arrived at from comparing the calorific units are correct, then the accumulation of gums, caramel, glycinic acid and its humoid decomposition products in low grade molasses should cause the carbon content of the non-sugars in such molasses to be higher than it is in sirups made by sulfitation or by filtration over bone black. This was confirmed by the following determinations of carbon which were made by J. A. Fries upon the dried residues used for the determination of Calories:

Sample	1	2	3	6	7	8
Total carbon in solids, %	38.945	40.138	39.790	38.159	39.394	39.249

The percentages of carbon due to the invert sugar and sucrose in the moisture-free solids of the above 6 samples, as calculated from the results of Table IV, are as follows

Sample.	1	2	3	6	7	8
Carbon in invert sugar, %	7.920	7.950	6.840	15.084	13.136	11.208
Carbon in sucrose, % .	29.832	30.426	26.986	19.126	21.479	19.829
Carbon in sugars, %	37.752	38.376	33.826	34.210	34.615	31.037

The percentages of carbon in the undetermined organic matter, found by subtracting the carbon in the sugars from the total carbon in the solids, are as follows

Sample	1	2	3	6	7	8
Carbon in organic non-sugars, %	1.193	1.762	5.964	3.949	4.779	8.212

From the above figures and the percentages of organic non-sugars in Table IV, the percentages of carbon in the organic non-sugars are computed to be:

Sample	1	2	3	6	7	8
Carbon in organic non-sugars, % .	28.27	40.32	48.17	40.97	42.74	49.00

The percentages of carbon in the organic non-sugars are thus seen to present the same relative order as that of the calories, being lowest in the cane juice and highest in the refinery molasses. The effect of bone black filtration in removing dehydration products of high carbon content is shown by comparing the low carbon percentages of Samples 6 and 7 with the high percentages of 3 and 8.

The percentages of carbon in the organic non-sugars as above estimated are probably in all cases too low owing to the retention of water of crystallization in the dried solids, as previously explained.

Conclusions.

In the manufacture of sirups and molasses from the juice of the sugar cane by the ordinary process of defecation with lime there is a progressive increase in the calorific value and carbon content of the organic non-sugars, owing to the formation of dehydration products such as caramel, glycinic acid and its humoid derivatives.

In the filtration of sirups and molasses over bone black there is a considerable removal of the lime salts of glycinic acid, the result being a lightening in color and a decrease in the calorific value and carbon content of the organic non-sugars.

In the manufacture of open kettle molasses by the sulfitation process, the formation of dehydration products is less pronounced than is the case by the defecation process, the result being a molasses of lighter color and with a lower calorific value and carbon content of the organic non-sugars.

The calorific value of the total solids in the sirups and molasses derived from the sugar cane was found to vary between 3.6 and 3.8 cals. per g. of dry substance, the average value being about 3.7 cals.

The calorific value of the organic matter in high-grade open-kettle sulfitation molasses and of high-grade refinery sirups was found to be about 3.9 Cals. per g. of dry organic substance.

The calorific value of the organic matter in sugar house defecation molasses and in refinery molasses was found to be about 4.0 Cals. per g. of dry organic substance.

The calorific value of the organic non-sugars in refinery sirups was found to vary between 4.04 and 4.16 Cals. per g. of dry substance.

The calorific value of the organic non-sugars in sugar house and refinery molasses was found to be 4.44 and 4.60 Cals., respectively, per g. of dry substance.

The carbon content of the total solids in the sirups and molasses derived from the sugar cane was found to vary between 38 and 40%, the average being about 39.5%.

The carbon content of the organic non-sugars in open-kettle and refinery sirups was found to vary between 40.32 and 42.74%.

The carbon content of the organic non-sugars in a sugar-house and refinery molasses was found to be 48.17 and 49.00%, respectively.

Finally, it may be noted that the results of this work have a certain bearing upon questions of nomenclature. It has been held by some that refinery sirups being a by-product of sugar manufacture should be termed molasses. But refinery sirups which have been filtered over bone black differ from defecation molasses so distinctly in the composition and calorific value of their organic non-sugars that in a chemical sense they cannot be grouped with such molasses.

In conclusion, the author desires to express his indebtedness to Mr. G. R. Bunker, of the National Sugar Refining Company, to Mr. H. E. Niese, of the American Sugar Refining Company, to Dr. G. L. Spencer, of the Cuban American Sugar Company, and to Dr. F. W. Zerban, of the Louisiana Experiment Station for furnishing him with samples of products. He is also under obligation to Mr. J. A. Fries, of the Pennsylvania

State College, and to his assistants, Mr. C. A Gamble and Mr. G. H. Hardin, for help in the analytical work.

NEW YORK CITY

[CONTRIBUTION FROM THE LABORATORIES OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH.]

THE ISOMERIC HYDROXYPHENYLARSONIC ACIDS AND THE DIRECT ARSENATION OF PHENOL.

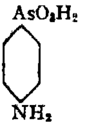
BY WALTER A. JACOBS AND MICHAEL HEIDELBERGER.

Received June 30, 1919

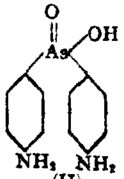
The present study of the action of arsenic acid upon phenol has demonstrated that this reaction is more complicated than has been heretofore assumed. As we shall set forth below, not only is *p*-hydroxyphenylarsonic acid formed in the reaction, but several other related substances as well.

Ehrlich and Bertheim,[1] in establishing the nature of the substance now known as arsanilic acid or *p*-amino-phenylarsonic acid (I), obtained by heating aniline with arsenic acid, drew the analogy between this substance and sulfanilic acid, obtained by a parallel method. As far as has been determined in these reactions, the substituent enters only the position *para* to the amino group It was then found that the method of direct arsenation was capable of extension to other simple aromatic amines with a free *para* position. Only in the case of a few *para*-substituted arylamines was it possible to force the arsonic acid into the *ortho* position and then only with great difficulty as evidenced by the very poor yields.

Benda,[2] and independently, Pyman and Reynolds[3] later found that this reaction did not stop at the formation of the primary arsonic acid but that this condensed further to an appreciable extent with a second molecule of the amine to form the secondary arsonic acid (II) in which the arsonic acid residue again entered the *para* position in the second arylamine nucleus.



(I)



(II)

The method of direct arsenation has also been extended to include the simpler phenols. According to the method outlined in *D. R. P.* 205616, in which phenol, *o*- and *m*-cresol are heated with arsenic acid, substances are obtained in which the arsonic acid residue enters the position *para* to the phenolic group. Further than this the patent does not go; and, as far as we are aware, more recent work has applied the reaction only to the arsenation of resorcin and its monomethyl ether.[1] From previous work, therefore, it would seem that the arsenation of phenolic compounds parallels that of the amines in that only *p*-hydroxy-arsonic acids have thus far been isolated.

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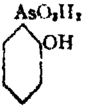
[1] *Ber.*, 40, 3292 (1907).

[2] *Ibid.*, 41, 2367 (1908)

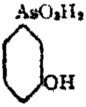
[3] *J. Chem. Soc.*, 93, 1184 (1908).

In connection with the preparation of *p*-hydroxy-phenylarsonic acid essentially according to the method outlined in *D. R. P.* 205616 we have had the opportunity of studying this reaction more fully. After isolating the *para* acid as the sodium salt, we were struck by the amount of material contained in the mother liquors which showed all the reactions of an aromatic arsonic acid and which obviously contained but relatively negligible amounts of the *p*-hydroxy acid. Furthermore, this mother liquor yielded an intense wine-red color with ferric chloride solution, whereas *p*-hydroxy-phenylarsonic acid gives no such color test. It therefore seemed likely that we were dealing with isomeric hydroxy compounds which were also products of the reaction. Just as the arsenation of aniline has been compared with the sulfonation of this base, it seemed also logical to compare the arsenation of phenol with the sulfonation of this compound. As is well known, depending upon the conditions of sulfonation, varying proportions of both *o*- and *p*-phenolsulfonic acids may be obtained.

Accordingly, in order to learn the properties of both *o*- and *m*-hydroxyphenylarsonic acids (III) and (IV), neither of which had hitherto been described, we prepared these compounds by diazotization of *o*- and *m*-arsanilic acids. Whereas phenol-*m*-arsonic acid resembled the *para* compound in giving no color test with ferric chloride, the phenol-*o*-arsonic acid gave the identical wine-red color observed with the mother liquors from phenol-*p*-arsonic acid.



(III).



(IV).

It was then found possible to isolate a basic barium salt from these mother liquors, which yielded a free acid identical with the hydroxy-compound obtained from *o*-arsanilic acid. The amount of this substance isolated was approximately $^1/_7$ of the yield of *p*-hydroxy-phenylarsonic acid. We hope by varying the conditions of the arsenation to determine whether or not the small yield is due to the migration of the arsonic acid residue from the *o*- to the *p*-position at the elevated temperature employed, a process which has been shown to occur in the sulfonation of phenol. We have not succeeded in isolating a *meta* acid from the mother liquors and it seems hardly likely on theoretical grounds that one should be formed in the arsenation of phenol.

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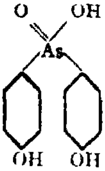
[1] Bauer, *Ber.*, 48, 509 (1915).

A comparison of the solubilities of the 3 phenolarsonic acids with those of the isomeric arsanilic acids proved interesting. Whereas in the latter series the *ortho* acid is most soluble and the *meta* compound the least soluble, with the former compounds the *o*-hydroxy acid unexpectedly proved to be the least soluble of the three. Thus it can be readily recrystallized from water without serious loss. There is little difference, on the other hand, between the solubilities of the *m*- and *p*-phenolarsonic acids.

We are continuing the study of the *o*- and *m*-hydroxy-phenylarsonic acids and their reduction products, nitro derivatives, etc.

On careful acidification of the mother liquor from the barium salt of the phenol-*o*-arsonic acid we were able to isolate two other substances, both of which gave analytical figures for the secondary dihydroxy-diphenylarsonic acids. These substances differed from one another in melting points and in the fact that in aqueous suspension one gave no color with ferric chloride solution, while the other, lower-melting substance, exhibited the same pronounced wine-red color so characteristic of phenol-*o*-arsonic acid. The higher melting acid possessed the same melting point as the *p,p'*-dihydroxy-diphenylarsonic acid (V), obtained according to Benda[1] by diazotization of *p,p'*-diamino-diphenylarsonic acid, and



(V)

agreed in other properties with this substance. We therefore conclude that our first substance is identical with Benda's compound.

The color reaction exhibited by our second substance indicates that it is a secondary *o*-hydroxy-arsonic acid. There are two substances which might possibly be formed in the arsenation of phenol and exhibit the properties of the isolated compound; *o,o'*-dihydroxy-diphenylarsonic acid (VI), and *o,p'*-dihydroxy-diphenylarsonic acid (VII).

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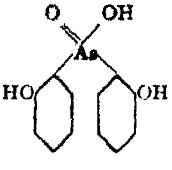
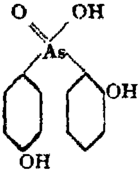
[1] *Loc. cit.*



(VI).



(VII).

Since the secondary arsonic acids no doubt arise from the reaction of a second molecule of phenol with the primary hydroxy-arsonic acids already formed, it is evident that VII could be formed in two ways: by the elimination of water between *o*-hydroxy-phenylarsonic acid and the *para* hydrogen atom of a second phenol molecule, or by the condensation of *p*-hydroxy-phenylarsonic acid with the *ortho* hydrogen of a second phenol molecule. VI, on the other hand, can only be formed from *o*-hydroxy-phenylarsonic acid which is present only in minor amounts. Therefore, since the yield of our second substance was approximately equal to that of the *p,p'* compound recovered, we are inclined to consider Formula VII as the more probable. We are at present attempting to establish the structure of the compound by other means. It also seems very likely that smaller amounts of VI are formed in the reaction and we are continuing the search for this substance.

The formation of the secondary acids extends the analogy to the sulfonation of phenol, since among the products of the latter is found dihydroxy-diphenylsulfone, and is likewise similar to the production of *p,p'*-diamino-diphenylarsonic acid in the arsenation of aniline. The formation of tertiary arsinoxides is likewise suggested, and we shall turn our attention to the possibility of isolating these among the products of the reaction. We shall also extend the study to the arsenation of other phenolic compounds, since similar products should result in the arsenation of the cresols, etc.

Finally, after the present work had long been under way, an article appeared by Conant[1] on the arsenation of phenol for the preparation of *p*-hydroxy-phenylarsonic acid. It will be seen that the conditions employed by us for the interaction of phenol and arsenic acid, with a few exceptions, are similar to those used by him and to those outlined in *D. R. P.* 205616, which, however, specifies "crystalline arsenic acid." However, it is entirely unnecessary in working up the melt to be satisfied with an impure sodium salt such as is isolated by Conant's method. As will be found in the experimental part of the present communication, and as has already been claimed by Kay,[2] it is a simple matter to obtain satisfactory yields of pure sodium *p*-hydroxy-phenylarsonate uncontaminated by other salts or by tarry by-products. As a matter of fact, the amount of tar formed in the method we have used is practically negligible and occasioned no difficulty. We are convinced that the direct arsenation of phenol is by far the simplest and most economical method for the preparation of this substance, so important in the manufacture of arsphenamine.

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[1] THIS JOURNAL, 41, 431 (1919).

[2] *Eng. pat.* 6,322 (1915).

EXPERIMENTAL.

(A) *o*- and *m*-Hydroxy-phenylarsonic Acids.

***o*-Hydroxy-phenylarsonic Acids.**—This substance was isolated in the direct arsenation of phenol as described in Section B, and in order to prove its structure it was also synthesized directly from *o*-arsanilic acid.[1]

11 g. of *o*-arsanilic acid were dissolved in 100 cc. of *N* hydrochloric acid, chilled, and diazotized with 50 cc. of *N* sodium nitrite solution. On standing at room temperature a steady, copious evolution of nitrogen occurred which was completed after an hour by gentle heating. The mixture was boiled with bone black, and the colorless filtrate treated with 50 cc. of *N* sodium hydroxide solution. On concentrating on the water bath the new hydroxy-phenylarsonic acid separated as a crust of long, stout needles. A few drops of dil. hydrochloric acid were added on cooling to insure proper acidity and the acid was filtered off and washed with ice water. The yield was 9.5 g. The acid is very easily soluble in hot water and forms supersaturated solutions on cooling, which rapidly crystallize when rubbed, yielding a mass of rosets of minute, colorless needles. When crystallization occurs slowly, as on concentrating its aqueous solutions, the acid separates as crusts of long, lustrous needles. Contrary to its *p*-isomer, it is rather sparingly soluble in cold water. The solubility relationships, therefore do not parallel those found in the comparison of *o*- and *p*-arsanilic acids, the latter being by far the less soluble.

o-Hydroxy-phenylarsonic acid is readily distinguished from the *para* compound by the color which it gives with ferric chloride solution. Whereas the *p*-isomer gives no color with this reagent even very dilute solutions of the *ortho* acid give a pronounced wine-red color. *m*-Hydroxy-phenylarsonic acid, described below, resembles the *para* compound in giving no color with ferric chloride, so that this reaction may therefore be used to distinguish the *ortho* acid from its isomers.

When rapidly heated to 185°, then slowly, *o*-hydroxy-phenylarsonic acid begins to soften at 185°, but is not completely melted until 196° is reached, then forming a liquid filled with bubbles. It is soluble in methyl or ethyl alcohol and but sparingly so in hot acetone or chloroform. Although difficultly soluble in glacial acetic acid, it dissolves readily on boiling. In alkaline solution, it couples readily with diazotized sulfanilic acid, yielding a bright orange solution. It is readily precipitated from concentrated solutions of its salts by hydrochloric acid, but redissolves on adding an excess. Acetic acid does not readily displace it from its salts.

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[1] This Journal, 40, 1583 (1918).

Subs., 0.3273 $Mg_2As_2O_7$, 0.2298.
Calc. for $C_6H_7O_4As$: As, 34.36. Found: 33.87.

Sodium Salt.—A suspension of the acid in a small amount of hot water was neutralized to litmus with strong sodium hydroxide solution and then treated with an equal volume of alcohol. The sodium salt, which separated on rubbing, was recrystallized from 50% alcohol, separating on standing in the cold as glistening, hexagonal platelets which contain 4 molecules of water of crystallization when air-dry. The salt is readily soluble in water and gives no immediate precipitates with calcium or barium salts but in the latter case, on rendering alkaline to phenolphthalein, what is probably a basic barium salt separates as rosets of colorless, microscopic needles. The heavy metals cause immediate flocculent precipitates.

Subs., air-dry, 0.7476 loss, 0.1713 *in vacuo* at 100° over H_2SO_4
Calc. for $C_6H_6O_4AsNa.4H_2O$: H_2O, 23.07. Found: 22.92
Subs., anhydrous, 0.2846 $Mg_2As_2O_7$, 0.1820.
Calc. for $C_6H_6O_4AsNa$: As, 31.20. Found: 30.87

***m*-Hydroxy-phenylarsonic Acid.**—This substance was prepared as follows from *m*-arsanilic acid.[1] 11 g. of *m*-arsanilic acid were dissolved in 100 cc. of 10% sulfuric acid, chilled and diazotized with a solution of 3.6 g. of sodium nitrite. The solution was diluted to 250 cc. and warmed to 60°, when a steady evolution of nitrogen occurred. When this had ceased, the sulfuric acid was completely removed with barium hydroxide solution. The filtrate was acidified with acetic acid, heated, and then treated with lead acetate solution as long as a precipitate formed. The lead salt separated at first in amorphous form, but rapidly changed to aggregates of microscopic platelets. After filtering off and washing, it was shaken with an excess of 10% sulfuric acid until completely decomposed. The filtrate from the lead sulfate was in turn treated with barium hydroxide solution until a test portion no longer showed the presence of dissolved barium and sulfate ions. The mixture was then treated with bone black and the clear, colorless filtrate boiled almost to dryness. The oily residue quickly crystallized on rubbing, giving 8 g. of the new arsonic acid. Recrystallized from a small volume of water and chilled to 0°, it separated as aggregates of rhombic crystals which melt slowly from 159° to 173°. It is readily soluble at room temperature in water, methyl and ethyl alcohols, and in boiling acetic acid. It is also somewhat soluble in hot acetone but practically insoluble in chloroform or benzene. It gives no color with ferric chloride solution and couples readily in alkaline solution with diazotized sulfanilic acid, giving a bright orange color.

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[1] THIS JOURNAL, 40, 1583 (1918).

Subs., 0.3045: $Mg_2As_2O_7$, 0.2135.
Calc. for $C_6H_7O_4As$: As, 34.36. Found: 33.84.

Sodium Salt.—A suspension of the acid in a very small amount of hot water was neutralized to litmus with sodium hydroxide solution. Since the salt could not be obtained by the addition of alcohol, it was allowed to evaporate and when almost dry, gradually crystallized in rosets of flat needles. It was too soluble to be recrystallized and acetone precipitated the concentrated aqueous solution as a pasty mass. For analysis this was dried *in vacuo* at 100° over sulfuric acid.

Subs., 0.2854: $Mg_2As_2O_7$, 0.1833.
Calc. for $C_6H_6O_4AsNa$: As, 31.20. Found. 31.00.

A solution of the salt gives no precipitates with barium or calcium salts but insoluble precipitates with those of the heavy metals.

(B) The Arsenation of Phenol.

p-Hydroxy-phenylarsonic Acid.—480 g. of 80% aqueous arsenic acid were boiled in an open flask, allowing the water to escape until the temperature reached 150°. Then 200 g. of molten phenol were poured in at once and an air condenser attached, the flask being then placed in an oil bath, the temperature of which was maintained at 155–60°. The contents of the flask boiled, rendering mechanical stirring unnecessary, and heating was continued for 7 hours. The air condenser acts as an efficient reflux avoiding undue loss of phenol. At the end the somewhat dark-colored liquid, which at first consisted of two layers, was homogeneous. It was diluted with about 2 liters of water, whereupon a small amount of tar precipitated, and, without filtering, a strong, hot solution of barium hydroxide was then added with vigorous stirring until the solution became just neutral to litmus, the unchanged arsenic acid being completely removed as the barium salt, which also efficiently collects the small amount of tar. It is important to avoid an unnecessary excess of barium hydroxide, since if the reaction becomes too strongly alkaline, the hydroxyphenylarsonic acids may also be precipitated. The clear, almost colorless filtrate from the copious barium arsenate precipitate was then treated with just enough sulfuric acid to remove the dissolved barium, a preliminary heating greatly facilitating the subsequent filtration of the barium sulfate. The precipitation is easily followed during the addition of the sulfuric acid by tests with filtered samples, and it is a simple matter to strike the point at which the filtrate no longer gives a test for either barium or sulfuric ion.

The filtrate was next concentrated to about a liter, preferably *in vacuo*, and then neutralized to litmus with sodium hydroxide. The solution of the salts was then concentrated further to small bulk, whereupon a partial crystallization of sodium p-hydroxy-phenylarsonate occurred. The mixture was heated until this was redissolved, a very small amount of water added if necessary; and then treated while still hot with several volumes of alcohol until a slight permanent turbidity was reached. On rubbing, the sodium salt quickly crystallized out, and after several hours of thorough chilling it was filtered off and washed with 85% alcohol. The yield averages about 120 g. and the colorless product so obtained is a practically pure sodium *p*-hydroxy-phenylarsonate giving no test for arsenate or sulfate ion and no color with ferric chloride solution. Hence it is seen that contamination with sodium sulfate, as occurs in Conant's method,[1] is an unnecessary complication.

Subs., air-dry, 0.6264: loss, 0.0781 *in vacuo* at 80° over H_2SO_4.
Calc. for $C_6H_6O_4AsNa.2H_2O$: H_2O, 13.04. Found: 12.46.
Subs., anhydrous, 0.2637: $Mg_2As_2O_7$, 0.1708.
Calc. for $C_6H_6O_4AsNa$: As, 31.20. Found: 31.26.

If it is desired to isolate the free *p*-hydroxy-phenylarsonic acid, the filtrate from the barium sulfate is concentrated *in vacuo* without the addition of sodium hydroxide, a thick syrup of a mixture of free arsonic acids being obtained. On dissolving this in several volumes of hot glacial acetic acid, a faintly colored solution is obtained which gradually sets to a thick paste of colorless crystals of *p*-hydroxy-phenylarsonic acid on chilling and rubbing. After standing 24 hours in the refrigerator it is filtered off and washed with small portions of cold glacial acetic acid. The yield of the arsonic acid, which melts at 170–3° with preliminary softening, averages 40 grams.

Subs., 0.2573: $Mg_2As_2O_7$, 0.1850.
Calc. for $C_6H_7O_4As$: As, 34.36. Found: 34.70.

Isolation of the substance as the sodium salt as first described is therefore preferable from the standpoint of yield. We have nothing to add to the properties of the acid and its sodium salt as already recorded in the literature.

***o*-Hydroxy-phenylarsonic Acid.**—The alcoholic mother liquor from the sodium salt of *p*-hydroxy-phenylarsonic acid was concentrated to remove the alcohol and then diluted to about 750 cc. with water. A few drops of this solution gave the intense wine-red color characteristic of *o*-hydroxy-phenylarsonic acid on treating with a drop of ferric chloride solution. The solution was treated with aqueous sodium hydroxide until strongly alkaline to phenolphthalein, and then with an excess of concentrated barium chloride solution. The barium salt of *o*-hydroxy-phenylarsonic acid separated as a heavy powder on rubbing, and an additional small quantity was obtained by heating the filtrate from this to boiling. The combined fractions of the salt were suspended in water and treated with dil. sulfuric acid in slight excess and then the excess of sulfuric acid precipitated by the addition of just enough barium hydroxide solution so that the filtrate contained neither barium nor sulfate ions. The colorless filtrate was concentrated on the water bath to crystallization, the *o*-hydroxy-phenylarsonic acid separating as a characteristic crust of long, lustrous needles. After thorough chilling, it was filtered off and dried. The yield was 14 g Recrystallized from hot water it formed flat, colorless needles which gave a wine-red color with ferric chloride solution, and proved identical in all respects with the substance obtained from *o*-arsanilic acid as described above A mixture of the substances obtained by both methods showed no alteration in the melting point.

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[1] *Loc. cit.*

Subs, 0 3279 $Mg_2As_2O_7$, 0 2310
Calc for $C_6H_6O_4As$ As, 34 36 Found 34 00

For further identification, it was converted into the sodium salt, which separated from 50% alcohol as hexagonal, microscopic platelets containing 4 molecules of water of crystallization, just as in the case of the salt prepared from the sample synthesized from *o* arsanilic acid

Subs, 0 6372 loss, 0 1475 *in vacuo* at 100° over H_2SO_4
Calc. for $C_6H_6O_4AsNa\ 4H_2O$ H_2O, 23 07 Found 23 15
Subs, anhydrous 0 2508 $Mg_2As_2O_7$, 0 1635
Calc. for $C_6H_6O_4AsNa$ As, 31 20 Found 31 48.

***p,p'*-Dihydroxy-diphenylarsonic Acid.**—The mother liquor from the barium salt of *o*-hydroxy-phenylarsonic acid was treated with hydrochloric acid until only faintly alkaline and then concentrated to about one liter. The chilled solution was then further treated with 1 1 hydrochloric acid, causing the separation of an oily precipitate which partly dissolved on further addition of the acid until definitely acid to congo red. On rubbing, crystallization slowly started, and on continued manipulation the oily precipitate also slowly solidified. After 4 hours' standing, the deposit was filtered off and washed with water. An aqueous suspension gave a wine-red color with ferric chloride due to contamination with another secondary arsonic acid to be described below On dissolving in hot 50% acetic acid and letting stand in the refrigerator, colorless, prismatic needles separated with a yield of 10 g., melting slowly with effervescence at 250–1° (uncorr) Benda[1] gives 239° as the melting point of *p,p'*-dihydroxy-diphenylarsonic acid obtained by diazotization of *p,p'*-diamino-diphenylarsonic acid. A sample of this substance prepared by us according to Benda also melted at 250–1° with effervescence, as did a mixture of this substance and that isolated as described above. Other properties were also identical. An aqueous suspension of the pure substance gave no color test with ferric chloride solution. It is practically insoluble in cold water, but dissolves appreciably on boiling and separates on cooling as short, colorless, prismatic needles. It is readily soluble in hot 50% or 95% alcohol or glacial acetic acid and in cold methyl alcohol, but very sparingly so in ether and acetone. Benzene and chloroform do not dissolve the substance. It is readily soluble in alkali and carbonate solutions and in 10% hydrochloric acid. In alkaline solution, it couples with diazotized sulfanilic acid, yielding an orange solution. There is no doubt that this substance is identical with that described by Benda as dihydroxy-diphenylarsonic acid.

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[1] Benda, *Ber.*, 41, 2371 (1908)

Subs., 0.2573 $Mg_2As_2O_7$, 0.1348.
Calc. for $C_{12}H_{11}O_4As$ As, 25.49 Found 25.30

o,p'(?)**-Dihydroxy-diphenylarsonic Acid.**—On standing several hours longer, the aqueous mother liquor from the *p,p'*-arsonic acid gradually deposited heavy aggregates of stout, glistening prisms which increased on rubbing. After about 48 hours, these were filtered off and washed with water. Four g. were obtained, melting at 215–6° with effervescence and giving a deep wine-red color with ferric chloride solution. The mother liquor was treated with sodium acetate solution until neutral to congo red, causing the precipitation of a small amount of resinous material. On standing, crystallization again started and was facilitated by rubbing. An additional 4 g. of material were thus obtained which also melted at 215–6° with effervescence and gave a deep wine-red color with ferric chloride solution. The combined fractions were dissolved in a small volume of hot 50% acetic acid and separated slowly on cooling as short, stout, glistening prisms which melted at 215–7° (uncor.) to a liquid filled with bubbles. Repeated recrystallization did not alter the melting point. A further small quantity of this substance was obtained on concentrating the 50% acetic acid mother liquor obtained in the recrystallization of the previously described *p,p'*-dihydroxy-diphenylarsonic acid and fractional recrystallization of the product so obtained. The compound is appreciably soluble in boiling water and separates on cooling as flat, glistening, prismatic needles. It is somewhat soluble in 50 or 95% alcohol, but quite readily so on boiling. It is also soluble in hot acetic acid and cold methyl alcohol, very sparingly in acetone and ether, and insoluble in benzene and chloroform. It dissolves readily in alkali and carbonate solutions and in 10% hydrochloric acid. In alkaline solution it couples with diazotized sulfanilic acid to yield an orange solution.

Subs., 0.2508. $Mg_2As_2O_7$, 0.1322.
Calc. for $C_{12}H_{11}O_4As$. As, 25.49. Found: 25.43.

The substance is readily distinguished from the *p,p'* isomer by the fact that in aqueous suspension it gives an intense wine-red color with ferric chloride solution, similarly to *o*-hydroxy-phenylarsonic acid. We, therefore, conclude that it is either *o,p'*-dihydroxy-diphenylarsonic acid or the *o,o'* isomer. Since *o*-hydroxy-phenylarsonic acid is now definitely established as a product of the arsenation of phenol, it seems likely that this substance may react with a second molecule of phenol to form the secondary arsonic acid, the arsonic residue entering the position *para* to the hydroxyl groups just as the *p,p'*-hydroxy compound results from the further alteration of *p*-hydroxy-phenylarsonic acid The yield of the acid also makes it seem probable that we are dealing with the *o,p'*-dihydroxy compound rather than the *o,o'* acid, as well as the additional possibility of its formation by condensation of *p*-hydroxy-phenylarsonic acid with a further molecule of phenol in the *o*-position. It is also probable that the *o,o'*-dihydroxy acid may occur among the reaction products but in such small amount as to render its isolation difficult. We are at present attempting to establish with certainty the identity of the new compound by synthetic means.

NEW YORK CITY.

[CONTRIBUTION FROM THE LABORATORIES OF THE ROCKEFELLER INSTITUTE FOR MED·CAL RESEARCH.]

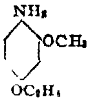
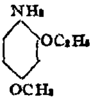
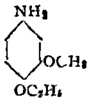
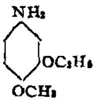
CERTAIN AMINO AND ACYLAMINO PHENOL ETHERS.

BY MICHAEL HEIDELBERGER AND WALTER A. JACOBS

Received July 5, 1919

In the course of recent chemotherapeutic studies it was found necessary to prepare as intermediates certain aromatic amines containing hydroxy, methoxy, and ethoxy groups, as well as multiples and combinations of these. While the monosubstituted compounds of this type have been adequately studied there are many gaps in the series of disubstituted amines containing the groups in question, as well as a number of inaccuracies in the descriptions of compounds which have already been prepared. In the present paper we have endeavored to fill some of these gaps and correct those inaccuracies which we have encountered, confining the discussion to certain amines and acylamino derivatives of anisole and phenetole and of the simpler mono- and di-ethers of pyrocatechol and resorcinol.

Of primary interest are perhaps the 4 isomeric methoxy-ethoxy-anilines:

M P				
The base	2 5–8°	22.5°	55°	81 5–2°
Acetamino deriv....	117 5–8 5	100 5–1	148 5–50	145–6
Chloroacetylamino deriv.	97 5–8	126–7	133–4	135 5–6

Of these the two derived from resorcinol have never been prepared, as far as we have been able to find, while the two amino-pyrocatechol ethers apparently were isolated as their hydrochlorides by Wisinger,[1] who also prepared the acetamino compounds and states that the free bases are easily oxidizable oils. Wisinger prepared the hydrochlorides and the acetyl derivatives by reduction of the two isomers obtained by nitrating pyrocatechol methylethyl ether, and designated the isomers by the letters α- and β-, being unable to determine which was the 3,4-methoxy-ethoxy- and which the 4,5-isomer. However, by ethylating 5-nitroguaiacol Paul[1] obtained a nitro ether corresponding to Wisinger's β-compound, whose β-methoxy-ethoxy-acetanilide would therefore be the 4,5-isomer, although the melting point given is considerably lower than that found by us for this compound. We have, on the other hand, found all four bases to be easily crystallizable and quite stable under ordinary conditions.

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[1] *Monatsh.*, 21, 1013 (1900).

It seems also that 3-methoxy-4-ethoxy-acetanilide was prepared by Freyss[2] by ethylation of a "*p*-nitroguaiacol" (m p. 104°), followed by reduction and isolation of the amine as the acetyl derivative. Freyss showed that the nitro group in his *p*-nitroguaiacol was in the position *para* to the hydroxyl group, so that his nitro ethyl ether should have corresponded to Wisinger's α-compound. It melted 20° higher, however, so that Wisinger's product would seem to have been either an *ortho* nitro derivative or a mixture, a conclusion borne out by the low melting point obtained by Wisinger for the acetamino compound as well. In any event, the methods employed in the present paper were such as to render it certain that no confusion between the isomers could arise.

Regarding the methods used, the substances containing the *p*-aminophenol grouping were prepared by reduction of the corresponding *p*-sulfophenylazo dye in ammoniacal solution by means of hydrogen sulfide, a method which we had used to good effect in the preparation of 4-aminoguaiacol.[3] Chloroacetyl derivatives were made according to the method devised by us and used in numerous instances already published.[4] All melting points above 140° are corrected to the short stem thermometer basis.

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[1] *Ber.*, 39, 2777 (1906).

[2] Freyss, *Zentr.*, 1901, I, 739

[3] This Journal, 41, 467 (1919)

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[5] *Loc. cit.*

New York City.

[Contribution from the Laboratories of the Rockefeller Institute for Medical Research]

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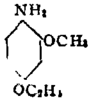
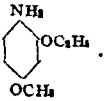
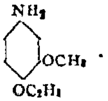
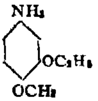
M P				
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[2] Freyss, *Zentr.*, 1901, I, 739.

[3] This Journal, 41, 467 (1919)

[4] *Ibid.*, 39, 1439 (1917) and subsequent papers.

[5] *Loc. cit.*

Chloroacetyl-*m*-anisidine.—The *m*-anisidine used in the preparation of this substance was prepared essentially as given by Reverdin and de Luc,[3] except that hydrolysis of the acetyl derivative was accomplished by boiling for $^1/_2$ hour with approximately 5 parts of 1 : 1 hydrochloric acid. Practically all of the base boiled at 131° under a pressure of 14 mm.

Six g. of *m*-anisidine were chloroacetylated in the usual way. The solution remained clear, but on chilling and rubbing in a freezing mixture it soon set to a solid cake. After adding 2 volumes of water the chloroacetyl compound was filtered off, dried, and recrystallized by dissolving in hot benzene, treating with $^1/_2$ volume of ligroin, and seeding. 6.9 g. separated as tufts of flat needles and long plates. Recrystallized again from absolute alcohol with the aid of a freezing mixture a portion melted constantly at 90.5–1.5° (corr.) with preliminary softening at 90°. It dissolves readily in the usual solvents with the exception of water and ligroin.

Subs., 0.3284 (Kjeldahl), 16.7 cc. 0.1 *N* HCl
Calc. for $C_9H_{10}O_2NCl$: N, 7.02. Found: 7.12.

Chloroacetyl-*o*-phenetidine, *o*-$C_2H_5OC_6H_4NHCOCH_2Cl$.—This substance was obtained in almost quantitative yield, separating as an oil on dilution of the reaction mixture with an equal volume of water and soon crystallizing. A portion was recrystallized twice from 85% alcohol, separating as hexagonal rhombs melting at 65.5–7.0° (corr.) with slight, preliminary softening. It is less soluble in alcohol and ligroin than in the other usual organic solvents.

Subs., 0.3200 (Kjeldahl), 14.7 cc. 0.1 *N* HCl
Calc. for $C_{10}H_{12}O_2NCl$: N, 6.56. Found: 6.44.

Chloroacetyl-*m*-phenetidine.—The *m*-phenetidine used for the preparation of this substance was prepared from *m*-acetaminophenol and diethyl sulfate in the presence of alkali at 50–60°, but the yield was not as good as that reported by Reverdin and Lokietek[4] using ethyl bromide. Practically all of the base boiled at 144.5° under a pressure of 20 mm.

The chloroacetyl derivative was obtained in almost quantitative yield as in the preceding cases, separating from the reaction mixture at once and forming so thick a paste that the addition of more 50% acetic acid was found necessary in order to maintain fluidity. After diluting with water a portion of the collected solid was recrystallized from 85% alcohol, then from toluene, forming flat, glistening needles, melting at 125.5–6.5°. The compound is readily soluble in acetone or chloroform, somewhat less easily in alcohol, ether or benzene at room temperature. It dissolves sparingly in cold toluene, easily on boiling, and is difficultly soluble in boiling water.

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[1] *J. Biol. Chem.*, 21, 135 (1915).
[2] *Arch. Pharm.*, 253, 233 (1915).
[3] *Ber.*, 47, 1537 (1914).
[4] *Bull. soc. chim.*, [4] 17, 407 (1915).

Subs., 0.2000: (Kjeldahl), 9.55 cc. 0.1 *N* HCl.
Calc. for $C_{10}H_{12}O_2NCl$: N, 6.56. Found: 6.69.

Chloroacetyl-*p*-phenetidine.[1]—This substance was also prepared in good yield as in the above cases.

3-Methyl-4-methoxy-acetanilide, 3,4-$CH_3(CH_3O)C_6H_3NHCOCH_3$.—Nineteen g. of *p*-amino-*o*-cresol[2] were dissolved in 170 cc. of *N* hydrochloric acid and the solution treated with 24.5 g. of acetic anhydride, followed immediately by 100 cc. of saturated sodium acetate solution. The mixture was shaken vigorously for 10 minutes and the precipitate of *p*-acetamino-*o*-cresol then filtered off and washed with water. The yield was 20 g. The crude product was converted into the methyl ether by dissolving in 1.1 equivalents of *N* potassium hydroxide solution and shaking with one equivalent of dimethyl sulfate, filtering off the ether and repeating the process with the filtrate with $^1/_4$ of the original amounts of alkali and dimethyl sulfate. The fractions were combined and a portion recrystallized from 50% alcohol, separating as large, nacreous, hexagonal scales which melted at 103–3.5° with slight preliminary softening. The compound is readily soluble in alcohol, acetone, chloroform, or ether, and dissolves sparingly in cold benzene, easily on boiling. It also dissolves with difficulty in cold water, more easily on boiling, the undissolved portions melting to an oil.

Subs., 0.1714. (Kjeldahl), 9.6 cc. 0.1 *N* HCl.
Calc. for $C_{10}H_{13}O_2N$: N, 7.83. Found: 7.85.

3-Methyl-4-methoxy-aniline.—The crude acetamino ether was boiled for one-half hour with 5 parts of 1 : 1 hydrochloric acid. The solution was diluted with water, chilled, and made strongly alkaline with sodium hydroxide. The 3-methyl-4-methoxy-aniline immediately separated in crystalline form and was filtered off, washed with water, and recrystallized from 50% alcohol. The yield obtained as outlined above from 30 g. of *p*-acetamino-*o*-cresol was 13 g., an additional 1.4 g. being obtained by dilution of the mother liquors of the recrystallization. The melting point was 59–9.5°, as given by Bamberger and de Werra,[3] who obtained the base by decomposition of *m*-tolyl-hydroxylamine with methyl alcohol containing sulfuric acid. The amine is easily soluble in alcohol, acetone, benzene, or ether, and dissolves very sparingly in cold water, readily on boiling, separating as an oil which crystallizes on rubbing. It may also be obtained from hot ligroin as thick, almost colorless, hexagonal plates. An aqueous suspension slowly gives a deep blue-violet color with ferric chloride, and the base is readily diazotized, coupling with R-salt to give a deep red color.

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[1] Bistrzycki and Ulffers, *Ber.*, 31, 2790 (1898); *Ger. pats.* 79,174, 84,654.

[2] Prepared according to THIS JOURNAL, 39, 2198 (1917).

[3] *Ann.*, 390, 175 (footnote) (1912).

3-Methyl-4-methoxy-chloroacetanilide.—The base was chloroacetylated as in the previous experiments, giving an excellent yield of the acyl derivative on diluting the reaction mixture with a little water and rubbing. A portion was recrystallized twice from 60% alcohol, then by dissolving in warm benzene and adding an equal volume of ligroin. It forms delicate needles melting constantly at 90–2° with preliminary softening, and dissolving readily in the usual organic solvents except ligroin.

Subs., 0.1524. (Kjeldahl), 7.15 cc. 0.1 *N* HCl.
Calc. for $C_{10}H_{12}O_2NCl$: N, 6.56. Found: 6.57.

2-Methyl-4-methoxy-aniline, 2,4-$CH_3(CH_3O)C_6H_3NH_2$.—Twenty g. of *p*-acetamino-*m*-cresol[1] were methylated as in the case of the *o*-compound. The yield of the acetamino ether was 14.5 g., agreeing in its properties with those recorded by Blangey,[2] who obtained the substance by acetylation of the amino compound. Thirteen g. of the acetamino ether were boiled for one hour with 65 cc. of 1 : 1 hydrochloric acid, diluted, chilled, and the solution made strongly alkaline with 25% sodium hydroxide solution. The oily base was extracted with ether, and after drying over sodium sulfate the solvent was distilled off and the residue fractionated *in vacuo*. Nine g. of 2-methyl-4-methoxyaniline were obtained, boiling at 144–52° (almost all at 146–7°) under a pressure of 23 mm. The almost colorless liquid crystallized as diamond-shaped platelets on chilling. These melted at 13–14° (corr.), the melting point being unchanged on recrystallization from ligroin. Bamberger and Blangey,[3] who obtained the base by treating *o*-tolyl-hydroxylamine with methyl alcohol containing sulfuric acid, give the melting point as 29–30°. In other respects their description was confirmed.

Subs., 0.1459 (Kjeldahl), 10.65 cc. 0.1 *N* HCl.
Calc. for $C_8H_{11}ON$: N, 10.22. Found: 10.23.

2-Methyl-4-methoxy-chloroacetanilide.—On treating 8.7 g. of 2-methyl-4-methoxy-aniline with a mixture of 45 cc. of glacial acetic acid and 45 cc. of saturated sodium acetate solution what appeared to be the acetate of the base crystallized at once. A clear solution was obtained, however, after adding an additional 110 cc. of 50% acetic acid. The solution was then chilled and treated cautiously with 7.2 cc. of chloroacetyl chloride, with continued cooling and vigorous shaking. Precipitation of the chloro-

[1] THIS JOURNAL, 39, 2200 (1917).
[2] *Dissertation*, Zürich, 1903.
[3] *Ibid.*, also *Ann.*, 390, 174 (footnote) (1912).

acetyl derivative was completed by adding an equal volume of water. After recrystallization from 85% alcohol the yield was 11.5 g. Recrystallized again from toluene, in which the substance is very easily soluble at the boiling point and very sparingly so in the cold, it separates as hair-like needles which melt constantly at 134.5–5.5°. It is practically insoluble in cold water but dissolves appreciably on boiling. It is sparingly soluble in cold alcohol, easily on boiling, and dissolves readily in acetone or chloroform.

Subs., 0.1749 (Kjeldahl), 8.15 cc. 0.1 *N* HCl.
Calc. for $C_{10}H_{12}O_2NCl$: N, 6.56. Found: 6.53.

***m*-Nitro-*p*-anisidine (3-nitro-4-methoxy-aniline).**—This substance was prepared by nitrating acet-*p*-anisidide according to German patent 101,778 and saponifying by boiling the nitro derivative with 25% sulfuric acid for 1/2 hour. The resulting solution was diluted with water, cooled somewhat, and made strongly alkaline. The base was extracted with ether, the solvent distilled off, and the residue dried on a porous plate. The crude product was dissolved in cold benzene and recrystallized by cautiously adding ligroin and rubbing. 16 g. of acet-*p*-anisidide gave 10.4 g. of the nitro-anisidine, melting at 55–7° and not at 50° as stated in the patent. Recrystallized twice from toluene, cooled, and treated with bone black the first time to remove a slight turbidity, the compound separated slowly as a hard crust of red prisms which melted constantly at 57–7.5° (corr.). As so obtained, the substance still contained a small amount of an amorphous residue which could be removed by dissolving in hot ether, filtering from the residue, adding ligroin, and letting the ether evaporate gradually. The nitro-anisidine gradually separated as orange-red prisms and plates which melted as above. It is readily soluble in the cold in acetone, alcohol, or ether, rather less so in benzene, and difficultly in cold toluene or water, readily on boiling. It dissolves in warm 10% hydrochloric acid with a pale yellow color, the hydrochloride separating on cooling as almost colorless, glistening platelets. It is readily diazotized, giving a sparingly soluble, orange-red dye with R-salt.

Subs., 0.1182: 16.6 cc. N (19.5°, 760 mm.).
Calc. for $C_7H_8O_3N_2$: N, 16.67. Found: 16.40.

3-Nitro-4-methoxy-chloroacetanilide.—Five g. of the nitro-anisidine were dissolved in 25 cc. of glacial acetic acid and chloroacetylated in the usual way after adding 25 cc. of saturated sodium acetate solution. The acyl derivative separated during the reaction and was filtered off after adding several volumes of water. The yield was 6.7 g. A portion was recrystallized from alcohol, then twice from ethyl acetate, in which it is rather difficultly soluble, forming golden yellow, flat needles melting at 149.5–51.5°. The substance dissolves quite readily in cold acetone and is somewhat soluble in cold chloroform, more easily on boiling. It is very difficultly soluble in cold water but dissolves appreciably on boiling.

Subs., 0.1284. 12 5 cc. N (19.5°, 766 mm).
Calc. for $C_9H_9O_4N_2Cl$ N, 11.46 Found· 11 46

3-Acetamino-6-methoxy-benzenesulfonic Acid.—Thirty g. of 3-amino-6-methoxy-benzenesulfonic acid (prepared by sulfonating *p*-anisidine[1]) were pulverized, dissolved in 147 cc. of *N* sodium hydroxide solution and shaken vigorously for 10 minutes with 18.2 cc. of acetic anhydride. The solution was then concentrated to dryness *in vacuo* and the residue taken up with acetone, filtered off, washed with acetone, and dried.[2] The yield of crude sodium 3-acetamino-6-methoxy-benzenesulfonate was 41.3 g.

A portion of the salt was dissolved in 2 parts of hot water and the solution treated with bone black and filtered. On adding to the filtrate an equal volume of 10% hydrochloric acid and rubbing the acid separated quickly as microscopic rhombs. These were filtered off, washed with a little 10% hydrochloric acid, and recrystallized from a small volume of water containing a few drops of acetic acid. The acid separated on cooling and seeding as minute, flat needles. When rapidly heated to 195°, then slowly, it intumesces at 197–8°, resolidifies, gradually turns yellow as the temperature is further raised, and finally melts again with gas evolution at about 250°. It is readily soluble in water and only sparingly in boiling methyl alcohol, ethyl alcohol, or acetic acid.

Subs., 0 1672 (Kjeldahl), 9 7 cc 0 1 *N* HCl.
Calc for $C_9H_{11}O_5NS$. N, 5 71. Found 5 80

3-Acetamino-6-methoxy-benzene-sulfonamide, $3,6\text{-}CH_3CONH(CH_3O)\text{-}C_6H_3SO_2NH_2$.—21 7 g. of the crude, dry sodium acetamino-methoxy-benzenesulfonate were intimately mixed in a mortar with 16.8 g. of phosphorus pentachloride, transferred to a flask with a drying tube attached, and heated for one hour at 50°. Hydrogen chloride was copiously evolved and at the end the flask was evacuated for about $^1/_2$ hour in order to remove as much of the phosphorus oxychloride as possible. The residue was then ground up with ice, filtered off when pulverulent, and the crude chloride allowed to stand for 2 days with 130 cc. of 1 : 1 ammonium hydroxide Nine g. of crude amide were obtained in this way, and the product was sufficiently pure for conversion into the amino amide. Analysis showed that recrystallization from alcohol was insufficient to ensure a pure product As obtained in this way the sulfonamide forms faintly yellow, radiating aggregates of minute, compact crystals which are only difficultly soluble in boiling alcohol When rapidly heated to 230°, then slowly, the substance melts to a dark liquid at 233–5.5°, with slow gas evolution.

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[1] Bauer, *Ber.*, 42, 2110 (1909).

[2] Cf. THIS JOURNAL, 39, 2428 (1917).

Subs., 0.2510 (Kjeldahl), 19.35 cc. 0 1 *N* HCl.
Calc. for $C_9H_{12}O_4N_2S$: N, 11 48. Found. 10.80.

3-Amino-6-methoxy-benzene-sulfonamide.—6.5 g. of the crude acetamino amide were boiled for $^1/_2$ hour with 35 cc. of 1:1 hydrochloric acid After cooling the solution was made just alkaline with ammonia and the precipitated amino-sulfonamide recrystallized from 50% alcohol. The yield was 3 4 g. Recrystallized again from 50% alcohol it separated from the cold, supersaturated solution as radiating, branched aggregates of minute, cream-colored spindles which melted at 184.5–6.0° with preliminary softening. It is difficultly soluble in the usual neutral organic solvents but dissolves readily in boiling water or 50% alcohol, less easily in boiling 95% alcohol. It dissolves in dil. hydrochloric acid or sodium hydroxide solution, the acid solution diazotizing readily and coupling with R-salt to give a deep red color. An aqueous solution gives a slowly developing brownish pink color with ferric chloride.

Subs., 0 1532 (Kjeldahl), 15 05 cc 0 1 *N* HCl
Calc. for $C_7H_{10}O_3N_2S$ N, 13.87. Found: 13.77.

(B) Derivatives of the Ethers of 4-Amino-pyrocatechol.

3,4-Methylenedioxy-chloroacetanilide, 3,4-$CH_2O_2C_6H_3NHCOCH_2Cl$.—Four g. of 3,4-methylenedioxy-aniline hydrochloride (from the nitro compound with tin and hydrochloric acid in dilute alcohol) were dissolved in 40 cc. of 50% acetic acid and 20 cc of saturated sodium acetate solution, chilled in ice-water, and treated with 3 cc. of chloroacetyl chloride. The resulting mixture was ground up in a mortar, diluted with an equal volume of water, and the precipitate filtered off and washed with water. After recrystallization from 85% alcohol the yield was 3.5 g., the substance forming both prismatic needles and glistening platelets. After 3 subsequent recrystallizations from toluene, in which it is easily soluble at the boiling point, but difficultly in the cold, the substance separated entirely as plumes of microscopic needles which melted constantly at 157 5–8 5° with preliminary softening. It is readily soluble in acetone, somewhat less easily in chloroform, and only sparingly in cold alcohol, readily, however, on warming. It also dissolves in boiling water and only very difficultly in the cold. The compound gives a pale yellow color with sulfuric acid.

Subs , 0 1503 (Kjeldahl), 7.0 cc. 0 1 *N* HCl
Calc. for $C_9H_8O_3NCl$: N, 6 56 Found 6.52.

4-Chloroacetylamino-guaiacol, 3,4-$CH_3O(HO)C_6H_3NHCOCH_2Cl$. —16.7 g. of 4-aminoguaiacol[1] were dissolved in a warm mixture of 100 cc. of acetic acid and 100 cc. of saturated sodium acetate solution, rapidly chilled, and cautiously treated with 15 cc. of chloroacetyl chloride. The resulting solution was concentrated to small bulk *in vacuo* and the crude, crystalline chloro-acetyl derivative recrystallized from a small volume of 50% alcohol. The yield was 17.5 g. Recrystallized from water with the aid of bone black, it forms slightly pinkish, thin, nacreous plates which melt at 113–4° with slight preliminary softening. The substance dissolves readily in acetone, alcohol, or hot water, less easily in hot benzene, and only sparingly in cold water or cold benzene. An aqueous solution gives a yellow-brown color with ferric chloride.

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[1] THIS JOURNAL, 41, 467 (1919).

Subs., 0.1554: 8.8 cc. N (28.5°, 755 mm.).
Calc. for $C_9H_{10}O_3NCl$: N, 6.50. Found: 6.37.

5-Chloroacetylamino-guaiacol, 3,4-$HO(CH_3O)C_6H_3NHCOCH_2Cl$. —5-Nitroguaiacol (m. p. 104°) was reduced according to Mameli.[1] After concentrating the detinned solution *in vacuo* and washing with a little 1 : 1 hydrochloric acid, the 5-aminoguaiacol hydrochloride (N, 7.83; calc., 7.98) formed practically colorless crystals which melted to a semifluid mass at about 160° and became completely fluid and decomposed at about 180° when rapidly heated. An aqueous solution gives a deep brown-red color with ferric chloride.

Six g. of the hydrochloride were dissolved in 25 cc. of water and chloroacetylated in the usual way after adding 10 cc. of acetic acid and 30 cc. of saturated sodium acetate solution. The substance crystallized on shaking and rubbing and was recrystallized from water containing a few drops of acetic acid, forming slightly pinkish hexagonal plates and prisms melting at 128–48° with preliminary softening. The yield was only 2.7 g., owing to considerable loss during the recrystallization. Two subsequent recrystallizations from toluene gave the melting point 140–50°, with preliminary softening, the compound forming pale pink, nacreous platelets. It dissolves in alcohol, ethyl acetate, boiling toluene, or boiling water, and is almost insoluble in cold toluene or benzene.

Subs., 0.1512: (Kjeldahl), 6.9 cc. 0.1 *N* HCl.
Calc. for $C_9H_{10}O_3NCl$: N, 6.50. Found, 6.39.

***p*-Sulfophenylazo-*o*′-ethoxy-phenol,** *p*-$HO_3SC_6H_4N.NC_6H_3(OC_2H_5)$-$OH(3',4')$.—23.1 g. of air-dry sodium sulfanilate (0.1 mol.) were dissolved in 400 cc. of ice and water, 7 g. of sodium nitrite added, and 60 cc. of 1 : 1 hydrochloric acid run in, with stirring. The resulting mixture was slowly added to a solution of 13.8 g. of *o*-ethoxyphenol (guethol), keeping the temperature at 20° by adding ice.[2] After stirring for 15 minutes, the deep orange-brown solution was acidified strongly with conc. hydrochloric acid. On rubbing and stirring the dye separated quickly as glistening, coppery aggregates of platelets. After letting stand overnight in the ice box the dye was filtered off and washed with 10% hydrochloric acid and then with acetone. The yield was 26.3 g. A portion was recrystallized from water, in which it is difficultly soluble in the cold, easily on boiling, forming dark red platelets with a purple reflex. After washing with a little water, then with acetone, and air-drying, the substance contained approximately 2 molecules of water of crystallization When rapidly heated the anhydrous compound melts and evolves gas at about 220°, with preliminary decomposition, while if the heating is slow above 200° it merely softens and gradually decomposes as the temperature is raised. The dye is readily soluble in methyl alcohol, less easily in absolute alcohol, changing to orange. It is somewhat soluble in boiling acetic acid, difficultly in cold water, the color changing to bright orange-red owing to formation of the hydrate. It dissolves readily in boiling water and gives a bright red color with conc. sulfuric acid.

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[1] *Chem. Centr.*, 1908, I, 25.

[2] Cf. the analogous preparation of 4-aminoguaiacol, *Loc. cit.*

Subs., air-dry, 0.3140: loss, 0.0338 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{14}H_{14}O_5N_2S.2H_2O$: H_2O, 10.06. Found. 10.76.
Subs., anhydrous, 0.1364: 10.55 cc. N (30.5°, 755 mm.).
Calc. for $C_{14}H_{14}O_5N_2S$: N, 8.70. Found: 8.64.

4-Amino-6-ethoxy-phenol, 4,6-$H_2N(C_2H_5O)C_6H_3OH$.—Seventy-two g. of the crude dye were dissolved in 720 cc. of 10% aqueous ammonia and treated with a rapid stream of hydrogen sulfide. The solution became hot, suddenly decolorized, and then began to deposit the aminophenol. After passing in hydrogen sulfide for $^1/_2$ hour the mixture was cooled with ice-water and the aminophenol filtered off and dried. The yield was 29 g. Recrystallization from 85% alcohol yielded an impure product, apparently owing to partial oxidation, so a portion of the substance was suspended in a little water, dissolved by adding hydrochloric acid, and the solution treated with sodium acetate. The resulting precipitate of dark, flocculent material was filtered off with the aid of bone black and the filtrate neutralized with sodium hydrogen carbonate. Under these conditions the compound separated as almost colorless, minute, glistening, hexagonal platelets melting to a deep brown liquid at 186–8° with preliminary darkening and softening. The aminophenol is readily soluble in hot acetone, less easily in the cold, and dissolves in boiling alcohol and only sparingly in the cold. It is rather sparingly soluble in boiling water and dissolves in alkali with a gray lilac color, changing to deep violet. An alcoholic solution gives an olive color with ferric chloride. The substance also turns purple with sulfuric acid, but dissolves with very little color.

Subs., 0.1493: (Kjeldahl), 9.7 cc. 0.1 *N* HCl.
Calc. for $C_8H_{11}O_2N$: N, 9.15. Found: 9.10.

4-Acetamino-6-ethoxy-phenol.—Twenty-nine g. of the crude aminophenol were dissolved in 145 cc. of warm 50% acetic acid, chilled in ice-water, and shaken with 23 g. (1.2 mols.) of acetic anhydride. The acetyl derivative crystallized on rubbing, and after diluting with a little water and letting stand in the ice box the collected product was recrystallized from 50% alcohol. The yield was 23.4 g. Recrystallized first from water containing a few drops of acetic acid, using bone black, then from 50% acetic acid, the acetaminophenol forms practically colorless, nacreous platelets which melt at 165.5–6.5° with preliminary softening. It is readily soluble in alcohol at room temperature, the solution giving an olive color with ferric chloride. It is very difficultly soluble in cold water, easily on boiling, an aqueous suspension giving an orange color with ferric chloride. The substance is soluble in warm acetone, sparingly in the cold, and is also slightly soluble in boiling benzene.

Subs., 0.1875. (Kjeldahl), 9 8 cc. 0.1 *N* HCl.
Calc for $C_{10}H_{13}O_3N$: N, 7 19. Found. 7.32.

4-Chloroacetylamino-6-ethoxy-phenol.—In this case it was necessary to add 6 additional parts of 50% acetic acid to the usual acetic acid-sodium acetate mixture before a clear solution could be obtained. The crude chloroacetyl derivative was recrystallized from 50% alcohol, in which it is easily soluble at the boiling point and only sparingly so a few degrees below. The yield was equal to the amount of aminophenol taken. Recrystallized again from boiling toluene it forms woolly needles which melt at 155–6° with preliminary softening. It dissolves readily in acetone and in boiling chloroform or alcohol, less easily in the last two in the cold. It also dissolves in cold methyl alcohol or boiling water, and is rather sparingly soluble in boiling toluene.

Subs , 0 1546· (Kjeldahl), 6 55 cc 0 1 *N* HCl.
Calc. for $C_{10}H_{12}O_3NCl$: N, 6 11. Found: 5.93.

4-Acetamino-guaiacol.—Forty g. of 4-aminoguaiacol[1] were dissolved in 200 cc. of 50% acetic acid and shaken with 1.2 molecular equivalents of acetic anhydride. The resulting solution was concentrated to dryness *in vacuo* and taken up in the minimum amount of water. The acetyl derivative crystallized on rubbing and letting stand, and was filtered off, dried, and recrystallized by dissolving in hot ethyl acetate, treating with bone black, and precipitating with the aid of ether. The yield was 25 g., the substance corresponding in its properties with that reported in the literature.[2] An additional amount was recovered by concentrating the mother liquors and adding ether.

4-Amino-veratrol.—12.5 g. of 4-acetaminoguaiacol were methylated in the usual way with dimethyl sulfate and potassium hydroxide solution, saturating with salt at the end to complete the separation of the acetamino-veratrole. This was filtered off, washed with a little ice-water, and saponified by boiling for 50 minutes with 25% sulfuric acid. The solution was chilled, made strongly alkaline, and the crystalline base filtered off and washed first with saturated sodium chloride solution, then with a little ice-water. The yield was 7.5 g., corresponding in its properties with those recorded in the literature.

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[1] *Loc. cit.*

[2] *Ber.*, 39, 3340; *Chem. Zentr.*, 1911, II, 1437.

3,4-Dimethoxy-chloroacetanilide.—Five g. of 4-amino-veratrol were chloroacetylated as in previous experiments. After recrystallization from 50% alcohol the yield was 6.2 g. Recrystallized from benzene it forms long, silky needles which melt constantly at 133.5–4.5° with slight preliminary softening. The compound dissolves readily in chloroform or acetone, rather sparingly in cold alcohol, easily on warming, and also dissolves in boiling water or boiling benzene.

Subs , 0 1655 (Kjeldahl), 7 35 cc. 0.1 *N* HCl
Calc. for $C_{10}H_{12}ONCl$ N, 6.11 Found: 6 22.

3-Methoxy-4-ethoxy-acetanilide, 3,4-$CH_3O(C_2H_5O)C_6H_3NHCOCH_3$.—16.7 g. of 4-acetamino-guaiacol were dissolved in the minimum amount of boiling water and treated with 95 cc. of *N* potassium hydroxide solution, the temperature dropping to 45°. Twelve g. of diethyl sulfate were then added in small portions, with vigorous shaking, the temperature remaining at 45–50° and the ether separating before all of the diethyl sulfate had been added. After shaking for a few minutes longer 50 cc. more of *N* potassium hydroxide solution were added, the temperature was raised to 50°, and the mixture then shaken with an additional 6 cc. of diethyl sulfate. After treating with aqueous ammonia to decompose any unchanged diethyl sulfate, the mixture was cooled, allowed to stand, and the product filtered off and dried. The yield was 15.8 g. A portion was recrystallized first from water, in which the colored impurities remained insoluble, and then from toluene, separating as long, narrow, nacreous plates which melt at 148.5–50° with slight preliminary softening. The compound separates from water as thick plates and columns. It also dissolves in alcohol or acetone at room temperature, and dissolves readily in hot benzene and freely, but slowly, in boiling toluene.

Subs , 0 1518· (Kjeldahl), 7.4 cc. 0.1 *N* HCl.
Calc. for $C_{11}H_{15}O_3N$. N, 6.70. Found. 6.83.

As stated in the introduction, this substance appears to have been obtained by Freyss.[1]

3-Methoxy-4-ethoxy-aniline.—14 5 g. of the acetamino compound were boiled for 55 minutes with 70 cc. of 25% sulfuric acid. The mixture was cooled, causing the sulfate to separate as large plates, and was made strongly alkaline and shaken out with ether. After drying the ethereal extract, concentrating, and fractionating the residue *in vacuo*, 6 g. of the base were obtained. It is a faintly yellow, very viscous liquid, which boils at 175–6° under a pressure of 20 mm. and soon solidifies to a mass of prismatic needles which show a solidification point of 55° (corr.) when the thermometer is placed in the crystallizing liquid. A few of the crystals, crushed on a porous plate, melted with preliminary softening at 55° to a turbid liquid which cleared completely at 59°. The crystalline base dissolves readily at room temperature in alcohol, benzene, or ether, and only sparingly in ligroin. It is difficultly soluble in water, the solution turning brown with ferric chloride and changing through wine-red to reddish purple on standing From a solution in an excess of dil hydrochloric acid the hydrochloride separates on chilling as very thin, nacreous scales It is readily diazotizable, the purple-red diazo solution (brownish green in thin layers) coupling with R-salt to give an intense purple red color.

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[1] *Loc. cit.*

Subs 0 1337 (Kjeldahl), 7 8 cc 0 1 *N* HCl
Calc for $C_9H_{13}O_2N$ N, 8 39 Found 8 19

3-Methoxy-4-ethoxy-chloroacetanilide.—3 5 g of the base were chloroacetylated in a mixture of 45 cc of 50% acetic acid and 15 cc of saturated sodium acetate solution. After diluting with water and washing the collected product the yield was 4 g. Recrystallized from a small volume of 50% alcohol, in which it is easily soluble at the boiling point and very much less so on cooling even a few degrees, the substance forms long, silky needles which melt slowly at 133–4° with slight preliminary softening It dissolves readily in acetone or chloroform, less easily in the cold in alcohol or benzene, and is fairly readily soluble in boiling water

Subs , 0 1586 (Kjeldahl), 6 7 cc 0 1 *N* HCl
Calc for $C_{11}H_{14}O_3NCl$ N, 5 75 Found 5 92

4-Methoxy-5-ethoxy-acetanilide, 4.5-$CH_3O(C_2H_5O)C_6H_3NHCOCH_3$ — Eighteen g of 4-acetamino-6-ethoxy-phenol (see p 1459) were dissolved in 100 cc. of *N* potassium hydroxide solution and the deep blue solution methylated in the usual way by means of dimethyl sulfate The methyl ether separated almost at once and the yield of crude product was 18 3 g A portion was recrystallized first from water, containing a few drops of acetic acid, using bone black, then from toluene, forming slightly purple, very thin, nacreous scales which melt slowly and constantly at 145–6° with preliminary softening. A mixture with the 3,4-isomer, which melts only a few degrees higher, softens and gradually melts above 115°, becoming entirely clear at 138°. The compound dissolves freely at room temperature in alcohol, acetone, or chloroform, and is sparingly soluble in cold toluene, easily on boiling. It is also difficultly soluble in cold water, but fairly readily so at the boiling point.

Subs , 0 1495 (Kjeldahl), 7 15 cc 0 1 *N* HCl
Calc. for $C_{11}H_{15}O_3N$: N, 6.70. Found 6 70

4-Methoxy-5-ethoxy-aniline.—17.5 g. of the acetamino compound were boiled with 10 parts of 25% sulfuric acid. The clear, dark purple solution was cooled in a freezing mixture, made strongly alkaline, and extracted with ether. After drying and concentrating, the crystalline residue was taken up in boiling benzene and the solution treated with ligroin until the initial turbidity barely disappeared. 10.2 g. of the base crystallized on seeding. Recrystallized from water with the aid of bone black, then from 50% alcohol, the substance separates slowly as faintly pinkish, rhombic crystals which melt constantly at 81.5–2° (corr.), with slight preliminary softening. It dissolves very easily in acetone or benzene, somewhat less readily in alcohol or ether, and only sparingly in 50% alcohol at 0°, but readily on warming. It is quite soluble in boiling water and rather difficultly in the cold, the aqueous solution gradually giving an intense violet color with ferric chloride. A solution of the base in 1 : 1 hydrochloric acid soon deposits the hydrochloride as delicate, colorless needles. In a dil. hydrochloric acid solution of the amine sodium nitrite gives a transient purple color, brown in thin layers, changing to brownish gray, and the substance couples with R-salt to give a deep red color.

Subs., 0.1688. (Kjeldahl), 10.3 cc. 0.1 *N* HCl.
Calc. for $C_9H_{13}O_2N$: N, 8.39. Found: 8.55.

4-Methoxy-5-ethoxy-chloroacetanilide.—5.1 g. of the base were dissolved in a mixture of 50 cc. of 50% acetic acid and 25 cc. of saturated sodium acetate solution, diluted with 100 cc. of 25% acetic acid, and treated with 4.3 cc. of chloro-acetyl chloride, with chilling and stirring. The chloro-acetyl derivative, which separated immediately, was filtered off and recrystallized from alcohol, the yield being 5.6 g. Recrystallized again from toluene it forms delicate, woolly needles which melt constantly at 135.5–6° with slight preliminary softening. It dissolves readily in acetone or chloroform, less easily in alcohol, and difficultly in cold toluene or benzene, but readily on boiling. It is rather sparingly soluble in boiling water. In its properties, therefore, it closely resembles the 3-methoxy-4-ethoxy isomer.

Subs., 0.1578 (Kjeldahl), 6.4 cc. 0.1 *N* HCl.
Calc. for $C_{11}H_{14}O_3NCl$: N, 5.75. Found: 5.68.

Diacetyl-4-amino-pyrocatechol.—Twenty-five g. of crude 4-aminopyrocatechol hydrobromide[1] were purified by solution in water containing a few drops of hydrobromic acid, treating with a few grams of stannous chloride, detinning with hydrogen sulfide, and concentrating the solution to dryness *in vacuo* The residue was taken up in 75 cc. of water, treated with 90 cc. of saturated sodium acetate solution, and shaken with 14 cc. (1.1 mols.) of acetic anhydride. The resulting mixture was cooled and filtered and the filtrate treated with solid sodium acetate and again shaken with 5 cc. of acetic anhydride. An additional amount of the diacetyl derivative separated and was filtered off, washed with a little water, and combined with the first fraction, the total yield being 14.4 g. Recrystallized twice from 50% alcohol containing a few drops of acetic acid, the substance separates as thin, glistening, faintly pinkish, hexagonal platelets which melt constantly at 187.5–92°. The compound dissolves readily in acetone, rather sparingly in 50% or 95% alcohol at room temperature, and difficultly in cold water, readily on boiling. An aqueous solution gives a grayish brown color with ferric chloride. An aqueous suspension dissolves on adding a drop of dil. sodium carbonate or ammonia, the solution in the latter case turning rosy-brown on shaking. When an aqueous suspension is warmed with sodium nitrite and a few drops of acetic acid the resulting clear solution deposits, on cooling and scratching, golden yellow platelets of a nitroso derivative which dissolves in alkalies with a brown-red color, changing rapidly to purple-red.

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[1] THIS JOURNAL, 41, 467 (1919).

Subs., 0.1598 (Kjeldahl), 7.85 cc. 0.1 *N* HCl
Calc. for $C_{10}H_{11}O_4N$: N, 6.70. Found: 6.88.

3,4-Diethoxy-acetanilide, $3,4\text{-}(C_2H_5O)_2C_6H_3NHCOCH_3$.—Thirteen g. of diacetyl-4-amino-pyrocatechol were suspended in about 150 cc. of water in a flask provided with a 3-hole stopper through which passed a gas delivery tube, an exit tube, and a dropping funnel. After the air in the flask had been displaced by hydrogen, 110 cc. of 2 *N* potassium hydroxide solution (a little over 3 mols.) were added through the dropping funnel, followed, after complete solution had taken place, by 16.5 cc. (2 mols.) of diethyl sulfate. The mixture was then warmed on the water bath, shaking continuously and passing in a stream of hydrogen. The diethoxy-acetanilide finally separated in crystalline form, after which 20 cc. of 5 *N* potassium hydroxide solution and 9 cc. of diethyl sulfate were added and the mixture again shaken and heated. After all of the diethyl sulfate had apparently been used up ammonia was added and the mixture allowed to cool slowly. It was finally chilled in ice, filtered, and the crude product recrystallized from a small volume of 50% alcohol. The yield was 4.9 g., agreeing in all of its properties with the substance as obtained by the alternative method described below and causing no sensible depression of the melting point when mixed with this.

4-Acetamino-6-ethoxy-phenol (see p. 1459) was ethylated in exactly the same manner as described for the ethylation of 4-acetamino-guaiacol (see p. 1460). The yield of crude 3,4-diethoxy-acetanilide obtained in this way was slightly more than the amount of starting material used, and this method is therefore recommended when guethol is available, as it is more direct and the yield is better. Recrystallized from 50% alcohol it forms nacreous platelets which melt at 124–5.5° with slight preliminary softening, thus agreeing with the description given by Wisinger,[1] who obtained the compound by reduction of nitro-pyrocatechol diethyl ether, acetylation of the amine hydrochloride, and saponification of the diacetyl derivative so obtained. Wisinger was unable to isolate the free base in a state of purity, but as will be seen below, this offers little difficulty.

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[1] *Monatsh.*, 21, 1015 (1900).

Subs., 0.1740: (Kjeldahl), 7.75 cc. 0 1 *N* HCl.
Calc. for $C_{12}H_{17}O_3N$ N, 6.28. Found· 6.24.

3,4-Diethoxy-aniline.—6.8 g. of the diethoxy-acetanilide were boiled for 15 minutes with 35 cc. of 1 : 1 hydrochloric acid, diluted with 2 parts of water, cooled somewhat, made strongly alkaline, chilled rapidly, and the mixture extracted with ether. The ethereal solution, when dried and concentrated, yielded 4 8 g. of the base as a crystalline residue. Recrystallized first by dissolving in benzene, adding ligroin, and letting stand in the ice box, then from a relatively large volume of ligroin, it separates as cream colored prisms, rhombs, thick plates, and needles which melt constantly at 47.5–8.5° (corr.). It is readily soluble in the cold in the usual neutral organic solvents with the exception of ligroin, and is also appreciably soluble in cold water. The aqueous solution gives an intense violet color with ferric chloride. When the base is dissolved in warm, dil. hydrochloric acid, the hydrochloride separates on cooling as delicate needles. A solution of the salt gives a purple color with sodium nitrite, coupling with R-salt to give a purple-red color.

Subs., 0.1513: (Kjeldahl), 8 4 cc 0 1 *N* HCl.
Calc. for $C_{10}H_{16}O_2N$ N, 7 74. Found. 7 78.

3,4-Diethoxy-chloroacetanilide.—The base was dissolved in a mixture of 15 parts of 50% acetic acid and 3 parts of saturated sodium acetate solution and chloroacetylated in the usual way. Precipitation of the chloroacetyl derivative was completed by dilution with water. Recrystallized first from 85% alcohol, then from toluene, it forms hair-like needles which melt at 122.5–4.5° with slight preliminary softening and resolidification a few degrees below the melting point. The substance dissolves readily in acetone or chloroform, less easily in cold alcohol, and only sparingly in cold toluene although very readily on boiling. It is practically insoluble in cold water, appreciably so on boiling, and dissolves in conc. sulfuric acid with a faint greenish yellow color.

Subs., 0.1529. (Kjeldahl), 6.15 cc. 0.1 *N* HCl.
Calc. for $C_{12}H_{16}O_3NCl$ N, 5.44. Found: 5.63.

(C) Derivatives of the Ethers of Resorcinol.

***p*-Sulfophenylazo-*m*-methoxy-phenol,** *p*-$HO_3SC_6H_4N : NC_6H_3(OCH_3)$-$OH(o',p'$-).—This substance was prepared exactly in the same way as was the *p*-sulfophenylazo-*o*-ethoxy-phenol described above (p. 1458), using 12.4 g. of resorcinol monomethyl ether. 25.2 g. of the dye separated as an orange-red crystalline precipitate on strongly acidifying the reaction mixture with hydrochloric acid. A portion of the dye was recrystallized from water, in which it is sparingly soluble in the cold, quite easily on boiling, separating as lustrous, brown-orange, lenticular platelets. After washing with water, then with acetone, and air-drying, the compound retained approximately one molecule of water of crystallization. The anhydrous substance forms a brick red powder which gradually darkens on heating and chars and swells at about 250°. It is fairly readily soluble in absolute alcohol, finally crystallizing out again on warming as short, thick, orange, microscopic plates. It is rather sparingly soluble in boiling acetic acid, a portion separating from the hot solvent in this case as well, apparently owing to combination with the solvent. The dye dissolves in conc. sulfuric acid with a yellow orange color, in dil. carbonates or alkalies with a reddish orange color.

Subs, air-dry, 0 2534 loss, 0 0163 *in vacuo* at 100° over H_2SO_4.
Calc for $C_{13}H_{12}O_6N_2S\ H_2O$ H_2O, 5 52 Found 6 43
Subs, anhydrous, 0 1293 9 8 cc N (24 5°, 770 mm)
Calc for $C_{13}H_{12}O_6N_2S$ N, 9 09 Found 8 82

4-Amino-5-methoxy-phenol, 4,5-$H_2N(CH_3O)C_6H_3OH$.—Twenty-four g. of *p*-sulfo-phenylazo-*m*-methoxy-phenol were dissolved in 240 cc. of 10% ammonium hydroxide and treated with a rapid stream of hydrogen sulfide until the solution became brown and the aminophenol was precipitated. After cooling, the precipitate, white at first, was filtered off and washed with water, rapidly turning gray on exposure to air. After drying *in vacuo* the yield was 7 6 g Recrystallized from boiling toluene, in which it is sparingly soluble, the base separates as delicate, pale purple-brown needles which darken when heated, blacken markedly at about 160°, and then soften, finally melting at 175–80° to a purple-black liquid. The substance dissolves in alcohol, but is very sparingly soluble in cold water, although readily on boiling, the solution turning purple in the air. An aqueous suspension gives a slowly developing brownish purple color with ferric chloride.

Subs, 0 1500 (Kjeldahl), 10 8 cc 0 1 *N* HCl
Calc for $C_7H_9O_2N$ N, 10 07 Found 10 08

The hydrochloride of this substance was obtained by Henrich and Rhodius[1] by reduction of nitroso-resorcinol monomethyl ether with stannous chloride, but the free base was not isolated The isomeric resorcinol derivative containing the amino group in the position *para* to the methoxy group, was obtained by Bechhold[2] by reduction of the phenol-azo-resorcin monomethyl ether formed on methylation of phenyl-azo-resorcinol.

4-Acetamino-5-methoxy-phenol.—4-Amino-5-methoxy-phenol was acetylated in 50% acetic acid solution by means of acetic anhydride. The resulting solution was concentrated to dryness *in vacuo* and the residue taken up in hot water and the solution treated with bone black and filtered. The acetyl derivative separated on standing overnight.

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[1] *Ber.*, 35, 1485 (1902).

[2] *Ibid.*, 22, 2378 (1889).

Recrystallized with the aid of bone black from water containing a few drops of acetic acid, then from toluene, which removes a black impurity, the acetaminophenol separates as pale pink aggregates of minute needles which begin to melt above 140° when slowly heated and finally melt completely at 169–71.5°. When rapidly heated the substance melts at 150–5°, resolidifies in a few moments, and then melts again at 169–71°. It is soluble in cold alcohol or acetone and dissolves rather sparingly in cold water, readily on boiling, separating on cooling as radiating masses or spears.

Subs., 0.1571 · (Kjeldahl), 8.70 cc. 0.1 *N* HCl
Calc for $C_9H_{11}O_3N$: N, 7.74. Found: 7.76.

4-Chloroacetyl-amino-5-methoxy-phenol.—Five g. of crude 4-amino-5-methoxy-phenol were dissolved in 60 cc. of 50% acetic acid and treated with bone black. The filtrate was treated with 25 cc. of saturated sodium acetate solution and chloroacetylated in the usual way. After recrystallization from 50% alcohol the yield of the acyl derivative was 5.1 g. Recrystallized again from ethyl acetate it forms practically colorless, nacreous platelets which melt constantly at 165.5–6.5° with preliminary softening. The substance is easily soluble in cold alcohol or acetone, also in boiling ethyl acetate or water, but sparingly in the cold. It is also very difficultly soluble in boiling chloroform.

Subs., 0.1534. (Kjeldahl), 7.25 cc. 0.1 *N* HCl.
Calc. for $C_9H_{10}O_3NCl$· N, 6.50. Found: 6.53.

***p*-Sulfophenylazo-*m*′-ethoxy-phenol.**—This substance was prepared exactly as given for the analogous dyes already described, using 13.8 g. of resorcinol monoethyl ether. The product separated slowly on acidifying strongly with hydrochloric acid, and was filtered off after standing in the refrigerator overnight, washed with ice-water and acetone, and dried. The yield was 25.4 g. Recrystallized from water, it forms flat, minute, glistening, brown orange, pointed needles and narrow plates with bevelled edges. After washing with acetone and air-drying, the substance contained approximately one molecule of water of crystallization. The anhydrous substance forms a brick-red powder which blackens at about 250–5° and softens on further heating, but does not melt below 285°. It is difficultly soluble in boiling absolute alcohol or acetic acid and is practically insoluble in boiling acetone. In sulfuric acid it gives a bright orange color. It dissolves rather sparingly in cold water with the same color, becoming slightly more red on adding alkali.

Subs., air-dry, 0.5054: loss, 0.0306 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{14}H_{14}O_5N_2S.H_2O$: H_2O, 5.30. Found: 6.06.
Subs., anhydrous, 0.1197: 9.05 cc. N (23.5°, 759 mm.).
Calc. for $C_{14}H_{14}O_5N_2S$: N, 8.70. Found: 8.70.

4-Amino-5-ethoxy-phenol. — *p*-Sulfo-phenylazo-*m*′-ethoxy-phenol was reduced by hydrogen sulfide in ammoniacal solution as in previous experiments. The yield of aminophenol was about 40% of the dye used. A portion was rapidly recrystallized from water containing hydrogen sulfide to suppress the oxidation which otherwise occurred, forming gray, glistening, microscopic leaflets which melt at 152–4° with preliminary softening and blackening. The compound dissolves readily in alcohol, less easily in cold acetone, readily on boiling, and is sparingly soluble in hot chloroform. It dissolves in boiling toluene with the exception of a few dark flocks, but on attempting to purify a portion of the substance by this method it darkened rapidly owing to oxidation. An aqueous suspension gives a purple color with ferric chloride, deepening to an intense violet, while a solution of the compound in dil. alkali rapidly turns dark purple and gives a dark purple precipitate.

Subs., 0.1530 (Kjeldahl), 10.0 cc. 0.1 *N* HCl.
Calc. for $C_8H_{11}O_2N$ N, 9.15 Found. 9.16.

4-Acetamino-5-ethoxy-phenol.—Twenty g. of 4-amino-5-ethoxy-phenol were dissolved in 240 cc. of 50% acetic acid, treated with bone black, and the filtrate shaken with 15.2 cc. of acetic anhydride. After several hours in the cold the acetaminophenol was filtered off and washed with water. The yield was 20.6 g., an additional 2.1 g. being obtained on concentration of the mother liquors. A portion was recrystallized first from 60% alcohol, then from 50% acetic acid, separating on seeding as pointed prisms of various shapes which melt slowly at 172.5–4.5° with preliminary softening, the melting point being unchanged by a subsequent recrystallization. The substance is fairly readily soluble in cold alcohol, acetone, or ethyl acetate, and is very difficultly soluble in cold water, although quite soluble on boiling.

Subs., 0.1839 (Kjeldahl), 9.3 cc. 0.1 *N* HCl
Calc. for $C_{10}H_{13}O_3N$. N, 7.19 Found 7.09

4-Chloroacetyl-amino-5-ethoxy-phenol.—4-Amino-5-ethoxy-phenol was chloroacetylated exactly as in the case of the 4,6-isomer (p. 1460). Recrystallized first from 50% alcohol containing a few drops of acetic acid, using bone black, the substance separates as gray, felted needles, while after a subsequent recrystallization from toluene it forms nacreous, feathery aggregates of gray plates which melt slowly at 158.5–61°. It dissolves readily in alcohol or acetone, less easily in chloroform, and is rather difficultly soluble in boiling water and practically insoluble in the cold. An alcoholic solution gives an olive color with ferric chloride.

Subs., 0.1523 (Kjeldahl), 9.45 cc. 0.714 *N*[1] HCl
Calc. for $C_{10}H_{12}O_3NCl$: N, 6.11. Found 6.20.

2,4-Dimethoxy-aniline, 2,4-$(CH_3O)_2C_6H_3NH_2$.—This substance was prepared by methylating 4-acetamino-5-methoxy-phenol with aqueous alkali and dimethyl sulfate and hydrolyzing the resulting 2,4-dimethoxy-acetanilide by boiling for $^1/_2$ hour with 1 : 1 hydrochloric acid, just as was done in the preparation of 4-amino-veratrole from 4-acetamino-guaiacol. The solution was made strongly alkaline and the base extracted with ether. After drying, this was concentrated to small bulk, the residue crystallizing in a freezing mixture. The product was melted, taken up in several volumes of ligroin, and the solution chilled and seeded. The base separated as nacreous, pinkish platelets which melted at 32.5–3.5° (corr.), the melting point being unchanged by subsequent recrystallization from a mixture of benzene and ligroin with the aid of a freezing mixture. According to Bechhold,[1] who prepared the base by reduction of phenyl-azo-resorcinol dimethyl ether, it melts at 39–40°. An aqueous solution gives a deep purple color with ferric chloride, while an alcoholic solution gives a green color, gradually changing to violet-brown.

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[1] Equal to $^1/_{14}$ normal.

Subs, 0 1226 · (Kjeldahl), 7.9 cc 0.1 *N* HCl.
Calc for $C_8H_{11}O_2N$ · N, 9.15 Found · 9 03

The hydrochloride of this substance was also prepared by Kauffmann and Kugel[2] by reduction of the nitro compound with tin and hydrochloric acid.

2,4-Dimethoxy-chloroacetanilide.—This compound was prepared from the base as in previous examples and recrystallized from 50% alcohol, the yield being almost quantitative. It forms delicate needles which melt at 89.5–90° (corr.) with slight preliminary softening. It dissolves readily in the usual organic solvents in the cold, with the exception of ligroin, in which, however, it is appreciably soluble in the cold and readily on heating. It is almost insoluble in cold water but dissolves fairly readily on boiling.

Subs., 0 1310 · (Kjeldahl), 5 7 cc. 0.1 *N* HCl.
Calc. for $C_{10}H_{12}O_3NCl$: N, 6.11. Found · 6.09.

2-Methoxy-4-ethoxy-acetanilide, 2,4-$CH_3O(C_2H_5O)C_6H_3NHCOCH_3$.—4-Acetamino-5-methoxy-phenol was ethylated by means of diethyl sulfate and aqueous potassium hydroxide in warm solution as described in previous examples. Recrystallized first with the aid of bone black from 25% alcohol containing a few drops of acetic acid, then by dissolving in hot benzene and treating the solution with an equal volume of ligroin, the substance forms pale pink, glistening platelets which melt slowly and constantly at 117.5–8.5° with slight preliminary softening. It dissolves readily in the cold in alcohol, acetone or chloroform, less easily in ether or benzene, and difficultly in ligroin or water. It is quite soluble in boiling water and dissolves in conc. sulfuric acid with a faint pink color.

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[1] *Loc. cit.*

[2] *Ber.*, 44, 2387 (1911).

Subs., 0.1536: (Kjeldahl), 10.25 cc. 0.0714 *N* HCl.
Calc. for $C_{11}H_{15}O_3N$: N, 6.70. Found: 6.67.

2-Methoxy-4-ethoxy-aniline.—The acetamino compound was hydrolyzed by boiling for $^1/_2$ hour with 1 : 1 hydrochloric acid and the base isolated by shaking out the alkaline solution with ether and fractionating the residue *in vacuo*. The yield was good. The amine forms a very viscous, practically colorless oil, which boils at 151.5–2.5° under a pressure of 12 mm and solidifies on chilling and rubbing. A portion was dissolved in a little benzene, diluted with ligroin, chilled, and let stand in the ice-box after seeding, separating as faintly pinkish rhombs which melt at 27.5–8.5° (corr.). It dissolves readily in the usual organic solvents, less easily in ligroin. It is quite soluble in water, the aqueous solution giving a violet purple color with ferric chloride, finally depositing purple, microscopic needles. The base dissolves in dil. hydrochloric acid, separating from a sufficiently concentrated solution on rubbing as needles and short prisms. It is readily diazotized, coupling with R-salt to give a deep, purple-red color.

Subs., 0.1860: (Kjeldahl), 15.35 cc. 0.0714 *N* HCl.
Calc. for $C_9H_{13}O_2N$: N, 8.39. Found: 8.25.

2-Methoxy-4-ethoxy-chloroacetanilide.—This compound was prepared as in previous examples. Recrystallized twice from a small volume of 85% alcohol, then from ligroin, it forms flat, narrow, striated plates which soften slightly at 97° and melt slowly at 97.5–8.0°. It is very easily soluble at room temperature in acetone, chloroform, benzene, or toluene, less readily in alcohol, and is almost insoluble in cold water, more easily on boiling.

Subs., 0.1615: (Kjeldahl), 9.15 cc. 0.0714 *N* HCl.
Calc. for $C_{11}H_{14}O_3NCl$: N, 5.75. Found: 5.66.

4-Methoxy-6-ethoxy-acetanilide, $4,6\text{-}CH_3O(C_2H_5O)C_6H_3NHCOCH_3$.—4-Acetamino-5-ethoxy-phenol (p. 1468) was methylated in the usual way with dimethyl sulfate and aqueous potassium hydroxide. When recrystallized first from 25% alcohol containing a few drops of acetic acid, with the aid of bone black, then from ligroin, the substance separates as faintly pink, silky needles which melt at 100.5–1.0° with slight preliminary softening. It dissolves readily in alcohol, benzene, or acetone, less easily in ether, and is very difficultly soluble in cold ligroin, more easily on boiling. It dissolves sparingly in cold water, quite readily on boiling. The substance gives a faint yellow color with conc. sulfuric acid.

Subs., 0.2209: (Kjeldahl), 14.9 cc. 0.0714 *N* HCl.
Calc. for $C_{11}H_{15}O_3N$: N, 6.70. Found: 6.75.

4-Methoxy-6-ethoxy-aniline.—11.3 g. of the acetamino compound were hydrolyzed with 1 : 1 hydrochloric acid. The chilled solution was decanted from the crystals of the amine hydrochloride, which were taken up in hot water and the solution cooled, made strongly alkaline, and shaken out with ether. After drying over potassium hydroxide and concentrating, the residue was fractionated *in vacuo*. 7.5 g. were obtained as a pale straw-colored, viscous liquid which boils at 144–4.5° under a pressure of 9 mm. and solidifies when chilled to a mass of thin platelets which melt at 22.5°. It is readily soluble in the usual organic solvents and dissolves appreciably in water at room temperature, readily on heating. An aqueous solution gives a brownish color with ferric chloride, changing to dark purple and giving a precipitate of the same color. In dil. hydrochloric acid it gives a bluish solution with sodium nitrite, but the solution contains the diazo salt, as it couples with R-salt to give a red color.

Subs., 0.1455. (Kjeldahl), 11.75 cc. 0.0714 *N* HCl.
Calc. for $C_9H_{13}O_2N$: N, 8.39. Found: 8.08.

4-Methoxy-6-ethoxy-chloroacetanilide.—The base was chloroacetylated in the usual way. Recrystallized from 50% alcohol, then from toluene, it forms thick, almost colorless, glistening platelets which melt at 126–7° with slight preliminary softening. It is very easily soluble in chloroform, quite soluble in acetone, and rather sparingly in cold alcohol, but readily on boiling.

Subs., 0.1517: (Kjeldahl), 8.45 cc. 0.0714 *N* HCl.
Calc. for $C_{11}H_{14}O_3NCl$ N, 5.75. Found: 5.57.

2,4-Diethoxy-acetanilide, 2,4-$(C_2H_5O)_2C_6H_3NHCOCH_3$. — 6.8 g. of 4-acetamino-5-ethoxy-phenol were ethylated as in previous experiments. The yield was 4.6 g., melting at 117–8°. Recrystallized from 50% alcohol, the diethyl ether forms silky needles of the same melting point. Will and Pukall,[1] who prepared the substance by reduction of phenyl-azo-resorcinol diethyl ether and acetylation of the amine hydrochloride, give 120.5° as the melting point. The compound is very difficultly soluble in cold water but dissolves quite freely on boiling, the undissolved portion melting to an oil.

2,4-Diethoxy-aniline.—The crude acetamino compound was hydrolyzed and the free base isolated as in previous examples. The residue from the ether extraction solidified on letting stand in a freezing mixture with occasional rubbing. It was again melted, taken up in a very little benzene, and diluted with several volumes of ligroin, chilled in a freezing mixture, and seeded. The base separated as pale brownish pink, flat needles and narrow platelets which melt at 33.5–4.0° (corr.) with preliminary softening. Will and Pukall give 32° as the melting point. The base seems quite stable in the air, and is smoothly diazotizable, coupling with R-salt to give a purplish red color. An aqueous solution gives a slowly developing, deep violet color with ferric chloride, followed by a precipitate of dark violet microscopic needles.

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[1] *Ber.*, 20, 1127 (1887).

Subs., 0.1330. (Kjeldahl), 7.3 cc. 0 1 N HCl.
Calc. for $C_{16}H_{15}O_3N$. N, 7.74. Found: 7 69

2,4-Diethoxy-chloroacetanilide.—One g. of the base was dissolved in a mixture of 5 cc. of acetic acid and 5 cc. of saturated sodium acetate solution, diluted with 30 cc. of 50% acetic acid, and chloroacetylated in the usual way. After dilution the product was filtered off and recrystallized from 85% alcohol, separating as delicate, woolly needles, which melt at 102–3° with slight preliminary softening. The substance is quite soluble in alcohol at room temperature, very readily in acetone, chloroform, or benzene. It is difficultly soluble in cold ligroin, readily on heating, and also dissolves sparingly in boiling water.

Subs, 0 1541· (Kjeldahl), 5 85 cc 0 1 N HCl.
Calc for $C_{12}H_{16}O_3NCl$ N, 5 44. Found· 5.32.

NEW YORK CITY

NOTE.

Correction.—In the paper on the "Constitution of Capsaicin," appearing in the July number,[1] vanillyl amine is by error described as 3-hydroxy-4-methoxy-benzylamine on pp. 1118, 1119, 1121, instead of 4-hydroxy-3-methoxy-benzylamine. E. K NELSON.

NEW BOOKS.

An Advanced Course in Quantitative Analysis. By HENRY FAY, PH D, D Sc John Wiley & Sons, Inc, New York, 1917 Pp. vi + 111

Text books on quantitative analysis may usually be placed in one of two groups; either the author has selected methods with reference primarily to the training of the student in the principles of quantitative analysis and in stoichiometry and has ignored the practicability of the methods described or else he has based his text book upon current and so-called "standard methods." In the latter case, too often, simplified manipulation, rapidity and occasionally great accuracy are the reasons for the selection of the material and the question of the effect upon the student of such a course is apt to be overlooked; the main idea being to have the student become proficient in the methods of analysis used in the industries.

Professor Fay has tried to produce a text which falls in neither extreme group. The material he has selected has been "chosen to illustrate principles and to train the student in manipulation." Since the author's work and interests lie mainly in iron, steel and commerical alloys, in which field he is a recognized authority, it is not surprising to find the bulk of the book devoted to the analysis of steel and closely associated raw and finished materials. Although the methods given have been selected with discriminating skill and are ably, accurately and minutely described, probably not a few teachers will question the soundness of a course in advanced quantitative analysis based entirely upon products of a similar nature (*e. g.*, ores and alloys). Even though the methods include varied manipulation there must perforce be a certain sameness of viewpoint and the student is not apt to acquire so satisfactory a foundation as if he were required to analyse materials of very different nature; for after all a course in advanced quantitative analysis should give the student something more than increased manipulative skill and stoichiometric ability.

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[1] THIS JOURNAL, 41, 1115 (1919).

It is, however, gratifying to find a text book in which the author has refrained from introducing all the numerical data and all the factors necessary for the calculation of results, leaving little for the student to do but go through the procedure like a machine. It is no wonder that the complaint is made that our young chemists do not know how to calculate the results of an analysis unless a text book is at hand. Professor Fay is to be congratulated upon his foresight in giving the student merely the necessary formulas and a few reactions and requiring him to compute his factors and calculate in full all his results.

The description of methods and details as to manipulation are clear and concise and are more comprehensive than are generally to be found in text books of this small size. The plan followed has been to give first in detail the method of procedure but with no reasons therefore or cautions as to difficulties to be encountered or possible sources of error. This concise description is in every instance followed by a series of excellent "Notes"—wherein the chemistry involved is discussed at length and full reference to the literature given. The bibliographic references are in fact a very valuable feature and raise the book to a plane somewhat above that of an ordinary text book.

The author has divided the subject matter into two parts. Part I—Mineral Analysis in which the following analyses are described and discussed: Determination of silica in a decomposable silicate, in a refractory silicate; determination of potassium and sodium in silicates (J. Lawrence Smith and perchloric acid methods); analysis of spathic iron ore; determination of sulfur in pyrite (4 methods); determination of titanium in titaniferous iron ore; Low's iodimetric determination of copper in copper ores; analysis of coal. Part II—devoted to the analysis of commercial alloys, includes phosphor-bronze; determination of carbon, manganese, phosphorus, sulfur, copper, nickel, chromium, tungsten, and vanadium in steel; determination of sulfur and of silicon in cast iron.

A table of atomic weights and a table of 4 place logarithms completes the book.

The pages are attractive with clear, black, legible type and are free from fine type and specially arranged paragraphs. E. M. CHAMOT.

A System of Physical Chemistry. 2nd Edition, in 3 volum[illegible]o III, Quantum Theory. (Text-books of Physical Chemistry, edited by Sir Wm. Ramsay.) By Wm. C. McC. Lewis, M.A. (R. U. I.), D.Sc. (Liv.), Brunner Prof. of Phys. Chemistry in the Univ. of Liverpool. Longmans, Green and Co., New York, 1919. viii + 209 pp., 14 figures. 14.5 × 22.5 cm. $2.50 net.

This is the third volume of Professor Lewis' "system" of physical chemistry. It presents a very complete survey of the numerous fields in which quantum theory has been applied.

The quantum theory itself is in a very shadowy stage of development, and Professor Lewis has attempted merely to bring together a complete account of existent work, rather than to clarify and sharpen the outlines of the theory itself. Perhaps this is all that can be done with profit at the present time, although I miss in this book such attempts at a logical development as were made by Planck in his original book, as have been made by Jeans (see for example the last edition of his "*Dynamical Theory of Gases*") or, at the risk of impertinence, as I have myself essayed ("A General Theory of Energy Partition with Applications to Quantum Theory").[1] The book does not even contain a complete mathematical development of the classical equipartition theory, from which quantum theory is a variant.

The enormous range of application of the quantum idea is well shown by Professor Lewis' collection of material. Thus we find the fundamental quantity "*h*" which first occurred in Planck's radiation formula, now occurring in all the various proposed formulas of Einstein, Nernst-Lindemann and Debye for the specific heat of solids, in Bjerrum's, Kruger's and Euchen's expressions for the specific heat of gases, in Bohr's treatment of the spectra of the elements, in all discussions of the photoelectric effect and the inverse photoelectric effect, in expressions for minimum ionization potential for gases, in calculations of the amount of radiant energy necessary to produce photochemical reactions, in expressions for the temperature coefficient of the rates of ordinary chemical reactions and in expressions for the mass action constant of ordinary chemical equilibria, etc.

The clearest cut example of the importance of "*h*" is of course the photoelectric effect, but it seems certain that whatever our final quantum theory becomes, the quantity "*h*" has permanently entered physical science and will be used in the treatment of many, if not all, of the phenomena listed above.

Professor Lewis' adequate collection of material from many sources makes the book an indispensable one for scientists who wish to assist in the clarification of the quantum theory.

It is interesting to note that the major part of the original work in this highly theoretical field has been done by Germans, much of it appearing during the war, and that the most important contributions to quantum theory from other sources comes from a group of brilliant Englishmen. Let us hope that this will argue for a future coöperative spirit in the affairs of science and the world. RICHARD C. TOLMAN.

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[1] *Phys. Rev.*, **11**, 261 (1918).

A Textbook of Physical Chemistry. By AZARIAH T. LINCOLN. D C. Heath and Co. 1918. vi + 547 pp 14 × 20 cm. $3 50

This book is intended primarily for beginners in the subject of Physical Chemistry and follows in general the usual lines for such texts. The author has found from his experience that it is necessary to review the fundamental concepts which have been given to the students in their elementary work. The first 7 chapters are mainly devoted to this purpose as well as parts of many other chapters. The author also recognizes that it has been necessary to exclude subject matter which he would gladly have presented, and presumably would have treated more exhaustively some subjects introduced had space permitted.

These difficulties seem to be generally experienced by teachers and text-book writers on Physical Chemistry. There is a tendency to go further back "to get a start," a situation which has resulted not from choice but from the necessity of getting results. Physical Chemistry deals with the theoretical and fundamental side of the science and should be introduced as early and as completely as possible in the elementary teaching and in all courses in chemistry. Due to the popularity of the subject, this has been done to an extent that is most gratifying to the physical chemist; but in view of experiences with third year students, one wonders whether there are not some real difficulties and particularly whether ideas have not frequently been introduced before a sufficient background of chemistry had been imparted to enable the student to grasp them. Certain it is that many of these students acquire a very superficial conception of important ideas which have been presented to them, and what is most unfortunate they often seem to have been rendered immune from gaining any real conception of these ideas. A revision of courses in general chemistry must give most careful consideration to this point and to the question of perspective so that the student may have some idea of the extent and importance of the various branches of the science. The students who elect the full course in chemistry are presumably the best of the beginners and most interested in the subject, so that for them little overlapping or repetition should be necessary.

The difficulties have been met by the author quite as well as in several of our recent text books; the derivation of the gas equation by a direct application of a theorem in variables is perhaps to be preferred to either of the two methods given and the experimental data and methods of arriving at the value of the unit volume of an ideal gas would be to the point as considerable and proper attention has been given to gas laws, kinetic theory and gas reactions. The various theories of solutions are presented with a chapter on concentrated solutions, one on hydration, and one on hydrolysis. There are chapters on thermochemistry, colloids, and rate of chemical reactions. The appendix contains an interesting collection of problems, many taken from the industrial world and arranged particularly for the convenience of the instructor. The author seems to have presented a very workable text-book. G. A. Hulett.

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A CRITICAL STUDY OF THE POTASSIUM AND SODIUM DOUBLE SALTS OF LEAD TETRAFLUORIDE AS SOURCES OF FLUORINE.[1]

BY GEORGE L. CLARK

Received April 9, 1919

The only strictly chemical method for the preparation of free fluorine which has shown satisfactory possibilities up to the present time is the decomposition of the double salt tripotassium lead hydrogen octafluoride $3KF.HF.PbF_4$, by heat. This compound was prepared in pure condition and studied for the first time by Brauner,[2] who showed that the molecule of hydrogen fluoride could be completely removed at temperatures below 250°, and that fluorine is evolved above 250°. In recent years doubts have been expressed by some chemists that such a discovery was really in accordance with the facts. By using this method, however, it has been found possible in the researches to be described in this paper to prepare quite successfully bromine trifluoride and iodine pentafluoride by permitting the fluorine evolved in the heating simply to pass over bromine and iodine, respectively.

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[1] Published by permission of the Director of the Chemical Warfare Service.

The general problem of the preparation and use of tripotassium hydrogen lead octafluoride was suggested by Captain A. B. Ray, and the investigations begun under his supervision and with the assistance of Messrs. I. M. Colbeth and J. H. Card, at the American University Experiment Station, Washington, D. C.

The intensive solubility measurements, and all of the work on disodium lead hexafluoride were subsequently carried on by the author independently.

[2] *J. Chem. Soc.*, 65, 393 (1894).

The double salt $3KF.HF.PbF_4$ was prepared, following the directions of Brauner by dissolving potassium plumbate (made by fusing potassium hydroxide with lead dioxide) in fairly concentrated hydrofluoric acid and evaporating off the excess aqueous acid. The double salt crystallizes from the concentrates in well-formed monoclinic needles. In the present work, however, it has been found that there are several factors influencing yield and purity of the salt which make the apparently simple process one of relative complexity. Several samples prepared under slightly differing conditions were found to give different analyses. In some cases when the salt was being used for the purpose of generating fluorine, all of the hydrogen fluoride could not be driven off below 250°, indicating contamination with potassium hydrogen fluoride which does not readily evolve hydrogen fluoride below 500°. This study was undertaken, therefore, to discover if possible, the exact conditions necessary for the preparation of pure tripotassium lead hydrogen octafluoride and what yields might be expected. It has involved the preparation and properties of potassium plumbate, and the determination of various solubility and hydrolytic effects. In addition to this, inasmuch as the scarcity of potassium hydroxide at once makes commercial applications of the process doubtful, the problem of substituting sodium hydroxide was undertaken. This has resulted in the isolation and study for the first time of the sodium double salt of lead tetrafluoride, as a source of fluorine. The steps in the preparation of both potassium and sodium salts will be considered in order and comparisons made.

The Preparation and Properties of Potassium and Sodium Plumbates.

In the preparation of tripotassium hydrogen lead octafluoride Brauner[1] directs that potassium hydroxide and lead dioxide be fused directly together in a silver dish in the proportion of 3 molecular weights of potassium hydroxide to one of lead dioxide. Experiments of the author show that when the hydroxide is brought to a clear melt at 360° and the lead dioxide then added in small quantities, reaction takes place and the final product is in the form of a stiff paste almost the color of lead dioxide, having the approximate composition of $3KOH.PbO_2$, or more nearly $K_2PbO_3.KOH$ since water formed according to the reaction

$$3KOH + PbO_2 = K_2PbO_3.KOH + H_2O$$

is driven off at the high temperature of the melt. At this temperature also there is apparently some decomposition as shown by 3 facts: (1)

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[1] *Loc. cit.*

a yellowish color due to the presence of lead oxide; (2) the formation of some potassium tetraoxide either alone or loosely combined which results in the evolution of oxygen when the plumbate paste is added to water or aqueous hydrofluoric acid; and, (3) the precipitation of an insoluble crystalline complex fluoroxyperplumbate from the solution in hydrofluoric acid.

This decomposition is due in part to the action of heat upon lead dioxide in its loose combination in this salt, causing a complete breaking of the molecule into its constituents and the reduction of PbO_2 to Pb_3O_4 and then to PbO by oxidation of K_2O to K_2O_4, and in part to hydrolysis at this high temperature of the potassium plumbate to potassium hydroxide and colloidal plumbic acid by the water formed in the reaction.

The addition of a third molecule of potassium hydroxide, besides making available the requisite proportions for the preparation of the potassium double fluoride, also, as a mass action effect, stabilizes the fusion. Sufficient liquid potassium hydroxide is formed to make it possible for all the lead dioxide to be stirred into a homogeneous fused paste without necessitating elevation of the temperature as high as 350°. It was deemed advisable to try the effect of adding water in small quantities to the hydroxide, resulting in a solution more properly speaking of water in molten potassium hydroxide which can remain liquid at 100°. With this solution lead dioxide reacts easily to form a homogeneous paste from which excess water may be driven at 100° without decomposition.

In the presence of water a somewhat different condition is found than in fusion of dry potassium hydroxide and dry lead dioxide. True potassium plumbate is really a salt of hexoxyplumbic acid, $H_2Pb(OH)_6$ or $PbO_2.4H_2O$, and has been obtained as $K_2PbO_3.3H_2O$ in the form of pure crystals from strongly concentrated solutions evaporated in a vacuum. This verifies the work of Fremy,[1] Seidel,[2] and Bellucci and Barravano.[3] It is found, however, that this salt is not a true hydrate, inasmuch as the 3 molecules of water cannot be driven off without completely decomposing the salt. This leads to the belief that the water is a necessary integral part of the molecule and that the formula is more properly $K_2Pb(OH)_6$. At temperatures below 100° the salt is entirely stable even in the presence of the excess potassium hydroxide. At 150° decomposition is apparent only by a lighter color of the surface exposed to air. Decomposition seems to take place according to the equation

$$K_2Pb(OH)_6 = 2KOH + PbO + O + 2H_2O.$$

It is at once clear, therefore, inasmuch as the molecular identity of $K_2PbO_3.3H_2O$ is fairly certain while the existence of K_2PbO_3 is very doubtful, that by using water in making the fusion of potassium hydroxide and lead dioxide and thus avoiding high temperatures, a plumbate of much more definite composition is possible. While it is true that reduction of the tetravalent lead to lower oxides is brought about at much lower temperatures if $K_2Pb(OH)_6$ is present, than in a fused mixture of dry lead dioxide and potassium hydroxide, yet it is found to be unnecessary to raise the temperature above 150°. Another advantage of adding water is found in the fact that much of the powerful corrosive property of an oxidizing agent fused with an alkali upon the containing vessel is avoided, since such action is a function of concentration and temperature. Porcelain dishes are most suitable for this purpose, since the glazing is only slightly attacked, while nickel and copper vessels are strongly corroded.

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[1] *Ann. chim. phys.*, [3] **12**, 488 (1844).

[2] *J. prakt. Chem.*, **20**, 200.

[3] *Z. anorg. Chem.*, **50**, 101 and 107 (1906).

Several experiments have been tried varying the amounts of water in the fusion. An amount not over $^1/_5$ the weight of the potassium hydroxide gives best results, while even $^1/_{10}$ permits homogeneous fusion below 200°.

Larger amounts of water exert a remarkably definite effect in hydrolyzing these compounds. For example, the action of water on $K_2Pb(OH)_6$ is

$$K_2Pb(OH)_6 + 2H_2O = 2KOH + H_2Pb(OH)_6$$
$$H_2Pb(OH)_6 = H_4PbO_4 + 2H_2O$$

or

$$K_2Pb(OH)_6 \rightleftarrows 2KOH + H_4PbO_4.$$

This proceeds from left to right preponderantly in the presence of 15 to 20% of water as indicated by the immediate precipitation of lead dioxide.

Sodium hydroxide acts quite differently from potassium hydroxide in its ability to form plumbates with lead dioxide. It has been shown already that by melting an excess of potassium hydroxide in water and adding lead dioxide, $K_2PbO_3.3H_2O$ may be obtained pure as crystals from the solution evaporated in a vacuum. There is only one statement to be found in the literature that any analogous sodium salt can be similarly prepared. Bellucci and Barravano[1] state that with great difficulty a very small quantity of powder was obtained which they thought to be the sodium salt. No analyses are given. Höhnel[2] claims that he obtained sodium plumbate by fusing together lead oxide and sodium peroxide, and that it is immediately hydrolyzed by water. It is quite clear that the sodium plumbates are very much less stable than the potassium. In this work it has been found mechanically impossible to fuse together dry sodium hydroxide and lead dioxide Impurities such as sodium carbonate in the caustic raise its melting point far above 318°. At such temperatures the lead dioxide is very rapidly reduced to plumboplumbic oxide and to lead oxide so that the resultant mass is simply a crumbling powder of a mixture of sodium hydroxide and lower oxides of lead Practically no plumbate is formed, as shown by the fact that the hydrofluoric acid to which the substance is added dissolves selectively only the sodium hydroxide together with a small quantity of both bivalent and tetravalent lead oxides. While lead fluoride is soluble to the extent of 0 6491 g per liter of water[1] no lead is detectable by any qualitative test in 50% hydrofluoric acid containing in solution more than 100 g. sodium hydrogen fluoride per 1000 g of water

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[1] *Loc. cit.*

[2] *Arch. Pharm.*, 232, 222 (1894).

In view of these difficulties all subsequent efforts to prepare plumbates of sodium have been made by means of very concentrated solutions of sodium hydroxide Enough water is necessary in order that all of the lead dioxide may be stirred in homogeneously Reaction occurs vigorously, forming first a greenish thin paste As more dioxide is added the color more nearly approximates the dark brown In any case the caustic solution is brought simply to boiling and the source of heat then entirely removed while the dioxide is being added Sufficient heat is generated by the reaction to keep the mass warm Temperatures above 100° cause rapid decomposition by combined action of the air and hydrolytic effect of the water present Even while the reaction is carried on over a water bath, the sodium plumbate once formed rapidly undergoes change.

In the belief that the sodium double fluoride of lead tetrafluoride might be entirely analogous to the potassium salt, $3KF.HF.PbF_4$, a number of fusions were undertaken using the proportion of 3 molecules of sodium hydroxide to one of lead dioxide With 150 g. of hydroxide and 300 g. of dioxide, it is found necessary for best conditions to add 75 g. of water, which is 50% of the weight of the caustic or 14% the weight of the total. Dissolving the sodium hydroxide in this and bringing to boiling, the source of heat is removed and the lead dioxide added with stirring The resultant mass is a homogeneous, almost solid paste. When this stands in air, or when any attempt is made to dry it in the neighborhood of 100°, rapid decomposition takes place. Using only 50 g. of water with the same mixture as indicated above results in the solidification of the mixture before all the lead dioxide is added. The mass is therefore heterogeneous and considerable dioxide lost when solution in hydrofluoric acid is made. More than 75 g. of water enables the plumbate to be prepared easily, but the paste is thinner, depending upon the amount of water used. The excess water serves then simply to dilute the hydrofluoric acid when solution is made, thus reducing materially the general efficiency of the acid in dissolving a maximum amount of the sodium double fluoride without hydrolysis.

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[1] Kohlrausch, *Z phys Chem*, 50, 365 (1904)

It is quite apparent that sodium plumbates are much less well defined and much less stable than the potassium salts. The experiments just described seem to indicate that in the presence of water the compound $Na_2PbO_3.6H_2O$ is formed chiefly, whereas the potassium salt is a trihydrate. The latter is quite stable at 100° while the sodium salt is quite rapidly decomposed at that temperature. Hydrolysis takes place immediately when water is added. Thus when making a fusion of 150 g. of sodium hydroxide, 300 g. of lead dioxide and 75 g. of water, the caustic is dissolved in 50 g. of water, the dioxide added until the paste is thick, and then the other 25 g. of water is added with the remainder of the oxide, a complete hydrolysis of the plumbate already formed is indicated by the separation of lead dioxide. But if all the water is introduced into the solution of sodium hydroxide before any additions of dioxide, reaction takes place without difficulty. This indicates that the water is therefore *not* water of hydration but an integral part of the molecule which is unstable enough to decompose easily at low temperatures. The presence of the excess molecule of sodium hydroxide, just as in the case of the potassium salt, has a stabilizing influence upon the fusion.

When as a result of careful analysis it was found that the sodium double fluoride of lead tetrafluoride contains only two molecules of sodium fluoride and is not therefore the analog of the compound $3KF.HF.PbF_4$, the preparation of sodium plumbate was begun, using 2 instead of 3 molecular weights of sodium hydroxide to one of lead dioxide. The proportions most satisfactory are sodium hydroxide 160, lead dioxide 478, and water 100. The reaction runs quite the same as before, the only difference noted being a somewhat smaller stability towards the action of heat and air. The effect of the excess hydroxide in the first fusions upon the solubility relationships and percentage yields of the double salt from hydrofluoric acid solution will be fully discussed in another section of this paper.

The outstanding conclusion of this study and comparison of the plumbates is quite favorable to the use of potassium plumbate for preparing a double salt from which fluorine may be driven by heat. Great care is necessary in order to prepare and keep sodium plumbate of fair degree of purity. In this connection it may be noted with interest that one of the methods of preparing lead dioxide is by the hydrolysis of sodium plumbate, Na_2PbO_3, which is made by fusing together lead oxide, sodium nitrate and sodium hydroxide.[*] With proper precautions, such as the proper amount of water and low temperature, $Na_2PbO_3.6H_2O$ may be prepared and used to advantage in forming the sodium double fluoride of lead tetrafluoride.

The Preparation and Properties of Tripotassium Lead Hydrogen Octafluoride.

In order to prepare this salt, the plumbate made as indicated in the preceding section is added a little at a time to strong aqueous hydrofluoric acid. Complete solution is observed at first but as the acid becomes weaker, some lead dioxide begins to separate out. At this point further addition of plumbate is stopped, since it would be decomposed, with separation of lead dioxide and solution of potassium hydroxide to form potassium hydrogen fluoride. This salt in turn decreases the solubility of the octafluoride in the aqueous hydrogen fluoride so that there is loss of material already dissolved. As the double salt dissolves, the solution warms. If the plumbate has been heated to too high a temperature and potassium tetraoxide formed, oxygen is evolved in the process of solution and a dark crystalline complex compound, probably a fluoroxyperplumbate, is precipitated even in the beginning.

After standing a short time in order to permit the lead dioxide and metallic fluoride impurities to settle, the solution is filtered through paper supported by several layers of cloth. The clear filtrate in lead dishes on sand baths is evaporated very gently in a stream of air. When crystals begin to form, the evaporation is carried on with extreme care. At this point there is great danger in obtaining crystals of the double salt contaminated with potassium hydrogen fluoride which remains in the mother liquor. If the addition of potassium plumbate has been carried only to the point where lead dioxide *just begins* to separate, the solution may very safely be evaporated to a very small residual volume with the possibility of only small contamination. It is essential, therefore, that an excess of hydrogen fluoride be kept always present. Very slight excess of plumbate after lead dioxide first begins to separate from the solution produces enormous solubility changes. In one instance 5 g. excess was added, the solution allowed to come to equilibrium, filtered and evaporated to dryness. The resulting pure white crystals upon analysis showed 24.22% lead while the pure octafluoride contains 43.4% lead. The mass is therefore almost half potassium hydrogen fluoride. Contamination with this salt is serious, inasmuch as the hydrogen fluoride cannot all be driven out below 250°, and therefore comes over with fluorine. It is true, however, that the hydrogen fluoride may be removed from the fluorine by passing the gases over fused potassium fluoride or through a condenser cooled with carbon dioxide-acetone mixture. In the preparation of the pure salt, $3KF.HF.PbF_4$, it is important, therefore, to separate as completely as possible the first crystals which form from the mother liquor.

Except for analysis of the double salt, Brauner's work on the octofluoride which is the only instance in the literature, was strictly of a qualitative nature. It was deemed advisable, therefore, to make as complete a study of this salt as possible with a view to controlling purity and yields.

Methods of Analysis.

The analysis of the complex salt once obtained presents no great difficulties. The most refined method for a quantitative determination of lead is to dissolve the double salt in strong nitric acid, the valence of lead thereby being reduced to two. The solution is diluted, sulfuric acid added and lead determined as the sulfate in the usual way. Potassium is determined as the sulfate in the filtrate by evaporating to fumes with excess sulfuric acid, and then igniting at a low red heat. In order to determine fluorine, another portion of the nitric acid solution and tripotassium lead hydrogen octafluoride is diluted and the lead precipitated as sulfide by hydrogen sulfide, some sulfur also being formed. The filtrate is made slightly alkaline with sodium carbonate and calcium chloride added in order to precipitate calcium fluoride.

In the course of these experiments, however, a very much simpler method of analysis has been found to be of great value as a time saver, at the same time being capable of a fair degree of accuracy. Water quantitatively hydrolyzes $3KF.HF.PbF_4$ according to the reaction

$$2(3KF.HF.PbF_4) + 4H_2O = 3K_2F_2 + 5H_2F_2 + 2PbO_2.$$

The lead dioxide precipitates out and may be filtered off and weighed as such. In some instances the product was collected on tared filter papers, but better results were obtained by the use of alundum crucibles. The dioxide is dried at 105°. Even at this temperature small amounts of water may be retained resulting in results slightly too high. This difficulty may be overcome by igniting to the monoxide and again weighing.

The filtrate is a solution of potassium fluoride in aqueous hydrogen fluoride. Part of it is titrated with standard alkali to determine fluorine as hydrofluoric acid formed by hydrolysis, together with the acid present as such in the original molecule. The rest of the solution is evaporated to complete dryness, ignited at 500° to decompose the potassium hydrogen fluoride and the residue weighed as potassium fluoride. These 3 very simple operations therefore enable the rapid determination of lead, fluorine and potassium.

In the preparation of samples of crystals of the pure double salt, of total solids, and of acid solutions for analysis, potassium plumbate carefully prepared as described was added in small quantities to aqueous hydrogen fluoride until the separation of lead dioxide became apparent.[1]

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[1] Commercial hydrofluoric acid analyzing 50% and containing hydrofluosilicic

The solution was then allowed to cool and to come to complete equilibrium by standing, and filtered. The clear filtrate was divided into several parts:

Part 1 was very carefully evaporated until well-shaped crystals began to form, and then placed in a vacuum desiccator until crystallization was complete. The crystals were removed from the mother liquor and dried repeatedly between filter papers. It is necessary that the operation proceed very rapidly as otherwise moisture in the air begins to cause darkening of the crystals by hydrolysis according to the equation

$$3KF.HF.PbF_4 + nH_2O = PbO_2.H_2O + 3KF.HF + 2H_2F_2 + (n - 3)H_2O.$$

The crystals so obtained were analyzed by the method outlined for lead, potassium and fluorine. The presence of one molecule of hydrogen fluoride was detected by titration after hydrolysis of the salt.

Part 2 of the solution was evaporated to complete dryness in order to determine the total double salt and the potassium hydrogen fluoride in solution. This was then subjected to complete hydrolysis, the lead dioxide filtered off, dried and weighed, and from the amount of lead so determined, the weight of the pure octafluoride was calculated. Subtraction of this value from the weight of the total solids gave the weight of potassium hydrogen fluoride. By titrating part of the filtrate from the lead dioxide for acidity and evaporating a part to dryness to determine potassium as potassium fluoride, a check could be established on the ratio of double salt to potassium hydrogen fluoride.

Part 3 of the solution was diluted with a large volume of water to complete hydrolysis, and the lead dioxide filtered off and weighed as a further check. The filtrate was then titrated with standard sodium hydroxide solution in order to determine what may be termed total acidity. This includes the concentration of hydrogen fluoride formed by the hydrolysis of the double salt and that of the acid in which the double salt is dissolved. Knowing the total solids in solution and having determined in Part 2 the so-called partial acidity, or the amount of hydrogen fluoride formed by their action with water, it was thus possible by subtraction to determine the strength of the acid solution and the amount of water present.

Part 4 of the solution was titrated carefully with water until a slight brownish tinge was apparent, indicative of incipient hydrolysis. This amount of water was then added to that known to be present in the solution as determined in Part 3 and the later concentration of free hydrogen fluoride in the solution thus determined. The solution was com-

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and sulfuric acids as impurities was used in these experiments. The use of acid of lower concentration is entirely impracticable as will be evident from the solubility data. Anhydrous liquid hydrogen fluoride cannot be used because of its immediate evaporation by the heat generated in the reaction.

pletely hydrolyzed, the lead dioxide filtered off and weighed and the filtrate evaporated to dryness. The residue was ignited to red heat and weighed as potassium fluoride. All evaporations and titrations were conducted in nickel or "Bario" vessels.

The results of these determinations are summarized in Table I, the divisions of which correspond to the 4 parts of the solution just described. The solubility relationships of the octafluoride and potassium hydrogen fluoride alone and together in hydrofluoric acid at different concentrations are shown in Table II.

TABLE I.

Analyses

	3KOH 1PbO$_2$ in H$_2$F$_2$		2NaOH 1PbO$_2$ in H$_2$F$_2$		3NaOH 1PbO$_2$ in H$_2$F$_2$
1. Pure crystals					
G. taken.. .	0 7433	0 3758 PbO_2 0 3233 PbO 0 4749 CaF_2	1 6770	1 1020 PbO_2 0 3840 (NaF)	
	0 6101	0 3088 PbO_2 0 2645 PbO 0 3330 K_2SO_4	2 7880	1 8885 PbO_2 0 6274 (HF)	
Calc. for $3KF.HF\ PbF_4$			($2NaF.PbF_4$):		
	3K	24 60	2NaF	22 89	
	Pb	43 35	Pb	56 40	
	8F	31 84	4HF	21 73	
			(Hydrolysis PbF_4)		
% composition					
Found . .	K	24 53	NaF	22 86	
	Pb	43 36 43 35	Pb	56 90 56 45	
	F	31 23	HF	21 80	
2. Solute. *a.* Total solids					
Wt. solution		6 3003	5 7067	23 4180	55 4120
Wt. dry residue.		0 8153		2 2775	4 1030
% solids................		12 94		9 726	7 40
b. Pure double salt:					
Wt. solid....		0 8153		1 2490	4.1030
Wt. PbO_2 from hydrolysis.		0 3545	0 3353	0 1845	1 8300
Wt pure, double salt. .		0 7075	0 6682	1 2020	2 810
% pure, double salt.		11 23	11 27	9 358	5 07
c. Alkaline acid fluoride					
Wt. in total solids (*a*) ...		0 1078		0 0470	1 293
% in solution		1 71		0 368	2 33
d. Normal fluoride (check).					
Calc. (double salt + acid fluoride)...............		0 3383			
Found............. ...		0 3367			
3. Solvent (original acid 49–50%):					
a. Partial acidity (hydrolysis of solids):					
Wt. solid......... .		0 8153		2 2775	4 1030
Wt. H_2F_2		0 1302		0 4900	0 7744
% H_2F_2...		1[illegible] 0	17 68 (calc.)	(17.87)	18.87

	$3KOH\ 1PbO_2$ in H_2F_2	$2NaOH\ 1PbO_2$ in H_2F_2	$3NaOH\ 1PbO_2$ in H_2F_2
b Total acidity (solvent + *a*)			
Wt solution	5.7067	12.8439	103.3280
Wt total solids .	0.7379	1.2490	7.6460
Wt $H_2F_2 + H_2O$	4.9688	11.5949	95.6820
Wt total H_2F_2 (titration)	1.5638	4.700	37.0645
c Solvent concentration (*b* — *a*)			
% H_2F_2	29.10	38.61	37.23
% H_2O	70.90	61.39	62.77
4 Solvent concentration at solute hydrolysis			
Wt solution	5.7067	12.8439	5.5650
Wt H_2O added to incipient hydrolysis .	3.50	5.85	20.0
Conc of H_2F_2 (%)	17.0	24.5	8.0

TABLE II

Solubility Relationships

a Solubility of K_2F_2 at 25° in 100 g of H_2O

G H_2F_2	% H_2F_2	G K_2F_2	% K_2F_2
0.0	0.0	96.3	48.0
1.61	1.5	61.0	37.5
6.05	5.7	30.4	22.3
12.5	11.1	30.5	21.3
16.0	13.8	33.4	22.3
20.7	17.2	38.4	24.1
28.6	22.3	46.9	26.7
42.0	30.0	61.8	30.0
100.0	50.0	136.0	40.5

b Solubility of $3KF\ HF\ PbF_4$ at 25° in 100 g H_2O

% H_2F_2	% K_2F_2	% salt
0	0	Hydrolyzes
29.1	1.71	11.23
30.0	0	12.21
17.0	1.71	Hydrolyzes
20.0	0	Hydrolyzes
20.0	25.0[1]	1.7

The Preparation and Properties of Disodium Lead Hexafluoride.

No record is to be found in the literature of the isolation and study of any double salt of sodium fluoride with lead tetrafluoride. Confronted by the necessity of substituting sodium hydroxide for the more expensive potassium hydroxide in preparing a salt to serve as the basis for obtaining fluorine, this study has necessitated the isolation and analysis for the first time of the double salt containing sodium. It seemed upon first thought that the formula of the sodium compound should correspond exactly to the potassium compound. Sodium plumbate was therefore prepared in the proportion of 3 molecular weights of sodium hydroxide to one of lead dioxide, observing the very particular conditions to prevent decomposition which have already been explained. Solution was made in hydrofluoric acid, the salt so formed analyzed and studied exactly as in the case of tripotassium hydrogen lead octafluoride. Repeated trials led to samples giving widely differing analyses so that it was impossible to calculate an exact formula. One sample analyzed according to the methods already described as used for the potassium double salt, contained 8.63% of lead, 32.37% sodium and 48.53% of fluorine, corresponding almost exactly to the formula $6NaF.4HF.PbF_4$. It soon was evident, however, that this sample was merely a large amount of sodium hydrogen fluoride containing a little of the true double salt. It was remarkably stable towards hydrolysis by water, was quite difficultly soluble and evolved hydrogen fluoride in amounts indicating the presence of sodium hydrogen fluoride. Another sample contained 14.46% of lead and 26.49% of sodium. It was reasoned from this that there must be excess sodium hydroxide in the plumbate which, when dissolved in hydrofluoric acid, resulted in the formation of sodium hydrogen fluoride along with the double fluoride of lead tetrafluoride, and that they could not be as easily separated from each other as are the corresponding potassium compounds because of the comparatively small solubility of sodium fluoride. The work of Marignac on the double fluorides of tin tetrafluoride furnished an analogy. This worker isolated tripotassium tin hydrogen octafluoride, which is isomorphous with the lead octafluoride, but found that the sodium compound was not analogous to the potassium, and possessed the formula $2NaF SnF_4$.

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[1] At higher concentrations of potassium hydrogen fluoride, lead dioxide itself is soluble.

Sodium plumbate therefore was prepared from sodium hydroxide and lead dioxide in the proportion of 2 to 1, and dissolved in 50% hydrofluoric acid until lead dioxide was just apparent. The crystals which formed were thick, short plates, instead of the needles of the potassium salt, and very much less stable. The salt was recrystallized 8 times, the crystals of sodium hydrogen fluoride which were first formed being rejected each time. By working very rapidly the plumbate crystals were separated from the mother liquor, dried between filters and weighed before they darkened. Analysis was made in the same way as outlined for the potassium salt. Solubilities and points of hydrolysis were also carried out in parallel with the determinations upon tripotassium lead hydrogen octafluoride. The results are summarized similarly in Tables I and III. Table I also shows the large influence upon solubility of the excess molecule of sodium hydroxide in fusions of $3NaOH + 1PbO_2$.

Attention is particularly called to the very remarkable effect of sodium hydrogen fluoride upon the solubility and hydrolysis of the double salt. The presence of 2.33% of the former, which lacks only 0.6% of being saturated, serves to diminish the solubility of $2NaF.PbF_4$ by over $^1/_2$

TABLE III.

Solubility Relationships

a. Solubility of Na_2F_2 at 25° in 100 g of H_2O.

G H_2F_2.	% H_2F_2 (solvent)	G. Na_2F_2.	% Na_2F_2 (solution)
0.0	0.0	4.2	4.03
1.0	1.0	4.14	3.9
4.6	4.4	2.25	2.1
8.4	7.7	2.3	2.0
13.0	11.5	2.4	2.08
59.6	37.3	4.88	2.9
77.7	43.7	8.2	4.5

Note: The solubility of sodium fluoride decreases with increasing concentration of hydrogen fluoride until sodium hydrogen fluoride is formed, followed by increase in solubility.

b. Solubility of $2NaF\ PbF_4$ at 25° in 100 g of H_2O

% H_2F_2.	% Na_2F_2.	% salt.
0	0	Hydrolyzes
38.61	0.368	9.358
40.0	Trace	10.49
24.5	0.4	Hydrolyzes
37.23	2.33	5.07
7.9	2.33	Hydrolyzes

(from 10.49 to 5.07) and to stabilize it towards the action of water by reducing the critical hydrolytic concentration of hydrogen fluoride from 24.5% to 8%. Another outstanding fact is that disodium lead hexafluoride is *more* soluble than is sodium hydrogen fluoride, although the solubilities are not greatly different, so that in fractional crystallization for separation, the pure, double salt *remains in the mother liquor.* The reverse relationships are observed in the separation of potassium hydrogen fluoride and tripotassium lead hydrogen octafluoride. The study of the very interesting 4 component system (H_2O-H_2F_2-$NaHF_2$-$2NaF.PbF_4$) will be continued further.

Comparison of the Potassium and Sodium Double Salts as Practical Sources of Fluorine.

Plumbates.—It has already been shown that potassium plumbate is more easily prepared, with more efficient use of the material. However, the greater availability and economy in the use of sodium hydroxide, especially inasmuch as the plumbate is prepared by fusing only 2 molecular weights instead of 3, may outweigh the mechanical and experimental difficulties.

Formulas.—If the salts could be prepared in pure condition exclusive of all other considerations, the advantage in the use of $2NaF.PbF_4$ over $3KF.HF.PbF_4$ as a source of fluorine is at once apparent, since no hydrogen fluoride must be driven from the molecule by preliminary heating.

Solubilities.—For a given weight of 50% hydrogen fluoride, the advantage is entirely on the side of the potassium salt, since under the most special conditions to avoid the formation of excess acid fluorides it is at least 4% more soluble than the sodium compound. There is manifestly much less difference between the solubilities of the double salts than between those of the fluorides (normal and acid salts, respectively).

In the second place, potassium hydrogen fluoride decreases the solubility of tripotassium lead hydrogen octafluoride far less than sodium hydrogen fluoride decreases that of disodium lead hexafluoride. This point deserves serious consideration, because even under the best conditions some of the acid fluoride will be present. The solubility of the potassium double fluoride is decreased only 1% by the presence of 2% of potassium hydrogen fluoride, while the solubility of the sodium compound is decreased $5^1/_2$% in a 2% solution of sodium hydrogen fluoride. Furthermore the potassium salt is in acid solution which is 10% weaker than the latter.

In the third place the potassium salt may be separated with ease from the contaminating potassium hydrogen fluoride by fractional crystallization, since the solubilities differ quite widely, whereas separation of the corresponding sodium compounds is almost impossible; indeed, the sodium hydrogen fluoride actually begins to crystallize out of solution first. There is a compensating advantage, however, in the fact that this compound gives up its hydrogen fluoride at temperatures considerably lower (160°) than does potassium hydrogen fluoride, so that even if hydrogen fluoride were evolved along with fluorine from the sodium double salt, it could be removed by condensation or absorbed in fused potassium fluoride.

Stabilities.—The pure potassium salt is considerably more stable than the pure sodium salt towards the action of moisture. In the invariable presence of the acid fluorides which exert a powerful stabilizing influence, however, there is little to choose between the salts in this respect.

Yields.—Weight for weight of materials used, the preparation of the potassium salt is almost twice as efficient a process as that of the sodium, as shown in the tables.

Recovery of By-products.—The evaporation of the saturated solutions to crystallization may be very successfully carried out as a distillation and the excess aqueous acid thus collected returned to the process. One sample so obtained from a solution of the sodium double salt analyzed 46.8% hydrogen fluoride. Similarly, the practically anhydrous hydrogen fluoride driven off at 250° may be condensed in a copper spiral cooled by carbon dioxide-acetone mixture and returned to the process. After fluorine has been evolved, salts of the formulas $3KF.PbF_2$ and $2NaF.PbF_2$ remain as residues. In either case the lead may be recovered as lead dioxide by dissolving in dil. nitric acid, filtering off any dioxide from the hydrolysis of unchanged lead tetrafluoride, adding alkaline hydroxide in excess and passing chlorine into the suspension of lead hydroxide below 50°. The precipitation of lead dioxide is practically quantitative according to the equation

$$PbO.H_2O + NaClO = PbO_2.H_2O + NaCl.$$

All fluorine remaining in solution may be recovered by precipitating as calcium fluoride which with sulfuric acid will regenerate the hydrofluoric acid used up. The entire recovery process as tested out on an experimental basis is 95% efficient.

Evolution of Fluorine.—The practically pure tripotassium lead hydrogen octafluoride has been used to advantage for the evolution of fluorine. Four hours at 250° usually suffice to drive off the hydrogen fluoride, and evolution of fluorine, as indicated by the formation of iodine crystals on potassium iodide paper, is evident at 300°. No experiments of this sort have been as yet possible with *pure* disodium lead hexafluoride because of the great difficulty in obtaining it pure. In every case the product has been contaminated with sodium hydrogen fluoride from which all the hydrogen fluoride could not be driven at 250°. There were strong indications of fluorine, however, from the salt even at 250°, so that undoubtedly the evolution from the pure salt would begin at quite low temperatures, which would of course be a distinct advantage.

NASHVILLE, TENN

[CONTRIBUTION FROM THE KENT CHEMICAL LABORATORY OF YALE UNIVERSITY]

ON THE SULFITE METHOD FOR THE SEPARATION AND DETERMINATION OF GALLIUM WHEN ASSOCIATED WITH ZINC.

BY LYMAN E. PORTER AND PHILIP E BROWNING.

Received July 19, 1919

The frequent occurrence of gallium with zinc makes the separation of these elements of especial importance. The usual method of separation consists in the precipitation of the gallium hydroxide by ammonium hydroxide in the presence of ammonium salts, the zinc remaining in solution.[1] This method has several disadvantages, for not only is it necessary to boil for a long time to expel the excess ammonia, in order that the precipitation may be complete, but in the process an appreciable amount of the gallium compound, the precipitate, usually adheres to the containing vessel; moreover, when extracting any considerable amount of gallium from material containing zinc, such as the leady residue from the purification of zinc or the gallium-indium alloy obtained from this

[1] Lecoq de Boisbaudran, *Compt. rend.*, 94, 1625 (1882).

residue,[1] the gelatinous nature of the gallium hydroxide results in slow filtration and a tendency to include a considerable amount of the soluble zinc salts even after several reprecipitations. Various procedures have been suggested to overcome these difficulties. Dennis and Bridgeman[2] precipitate the zinc by the use of potassium mercuric thiocyanate, leaving the gallium in solution; the mercury is then removed by hydrogen sulfide. The gallium is separated by boiling the solution with sodium sulfite in the presence of hydrochloric acid, or by using ammonium sulfite. Care must be taken, the authors state, to have the acid concentration right, otherwise some gallium is dissolved, either by the excess of acid or by the alkali formed by the hydrolysis of the sodium sulfite.

The work described in the present article has to do with a direct application of the sulfite method to the separation of moderate amounts of zinc from gallium. It is assumed that any indium originally present has been previously separated by sodium hydroxide and that the greater part of the zinc has been removed by precipitating the gallium hydroxide in the presence of ammonium chloride.[3,4] The reagents used are sodium hydrogen sulfite and ammonium hydrogen sulfite, formed by saturating, respectively, with sulfur dioxide a 10% solution of sodium sulfite and dil. ammonium hydroxide (1 : 4).

Preliminary experiments showed that 0.0002 g., or even less, of gallium can be precipitated in 5 cc. of solution by boiling with a drop or two of either of these reagents. Similar experiments on solutions containing zinc showed no precipitation even after boiling 10 minutes, although it may be precipitated from neutral solutions by neutral sodium sulfite. To test the completeness of the gallium precipitation, a study was made of the delicacy of the potassium ferrocyanide test,[5] with a view to using it to detect gallium in the filtrate after the sulfite precipitation. In hydrochloric acid solution as small an amount as 0.0001 g. of gallium in 5 cc. of solution can be detected by the ferrocyanide.[6] It was found, however, that if 0.002 g. of gallium in 5 cc. of solution is treated with ammonium hydrogen sulfite in the cold, no precipitate forms upon the addition of the ferrocyanide, nor does it come down on long standing. The addition of an excess of hydrochloric acid to this solution, however, causes precipitation. By the use of smaller amounts of gallium it was found that the delicacy of the test is not interfered with by the sulfite, provided that sufficient hydrochloric acid or other strong acid is present.

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[1] Browning and Uhler, and Uhler and Browning, *Am J Sci*, 41, 351 (1916); 42, 389 (1916).

[2] THIS JOURNAL, 40, 1531 (1918).

[3] Lecoq de Boisbaudran, *Loc cit.*

[4] Browning and Uhler, *Ibid.*

[5] Lecoq de Boisbaudran, *Compt. rend.*, 99, 526 (1884).

[6] Browning and Porter, *Am. J Sci.*, 44, 221 (1917).

This constitutes a difference between the behavior of gallium and that of zinc, because the latter may be precipitated as the ferrocyanide from a solution containing sulfite, even in the absence of strong acid.

A series of precipitations of gallium was made from neutral or slightly acid solutions by boiling them with ammonium hydrogen sulfite. Amounts of gallium ranging from 0.0005 g. to 0.005 g. calculated as the metal, were used. The filtrates from the precipitations were treated with hydrochloric acid and potassium ferrocyanide. Negative results proved the completeness of the precipitation.

The following procedure for the qualitative detection and separation of gallium and zinc was tried successfully on unknown solutions. The results are given in Table I. The neutral or slightly acid solution, about 5 cc., is boiled for two minutes with sodium hydrogen sulfite. A precipitate, indicating gallium, is filtered off after it settles. Hydrochloric acid is then added to the filtrate, followed by potassium ferrocyanide. A precipitate here shows the presence of zinc. Similar results were obtained by substituting ammonium hydrogen sulfite for the sodium salt. In the table, Expts. 11 to 13 are significant in that the failure to get a test with the ferrocyanide gives additional evidence that the precipitation of gallium is complete.

TABLE I

Qualitative Detection of Gallium and Zinc

Expt	Taken G.	Found	
1	Ga 0.0001	Ga present (doubtful)	Zn absent
2	Ga 0.0002, Zn 0.0015	Ga present	Zn present
3	Zn 0.001	Ga absent	Zn present
4	Ga 0.0002, Zn 0.0003	Ga present	Zn present
5	Ga 0.0003	Ga present	Zn absent
6	Zn 0.0002	Ga absent	Zn present
7	Ga 0.0002	Ga present	Zn absent
8	Zn 0.0005	Ga absent	Zn present
9	Distilled water	Ga absent	Zn absent
10	Ga 0.0003	Ga present	Zn absent
11	Ga 0.005	Ga present	Zn absent
12	Ga 0.0025 . .	Ga present	Zn absent
13	Ga 0.005	Ga present	Zn absent

This method lends itself well also to the quantitative estimation of gallium in the presence of zinc, on account of the granular form of the precipitate. The gallium is conveniently precipitated from 200 cc. of solution, which is neutral or slightly acid. After the addition of 4 or 5 cc. of ammonium hydrogen sulfite the solution is heated to boiling for from 3 to 5 minutes. At the end of this time the precipitate of gallium is in distinctly granular form and settles readily. The supernatant liquid is decanted through a filter paper. The precipitate left in the beaker is dissolved by the addition of a few drops of hydrochloric acid and 200 cc.

of water is added. The gallium is reprecipitated as before, and the precipitate is filtered off upon the original filter paper, ignited, and weighed as Ga_2O_3. It was found that if the gallium is not reprecipitated when zinc is present a somewhat high result is obtained, but this is obviated by a single reprecipitation.

Expts. 9 and 10, Table II, are of special interest, because in the former the gallium was reprecipitated 3 times, and in the latter twice, the results showing that this precedure does not result in any loss of gallium.

TABLE II

Quantitative Estimation of Gallium Precipitated by Ammonium Acid Sulfite

Expt	Amount $ZnCl_2$ taken G	Amount Ga_2O_3 taken G	Amount Ga_2O_3 found G	Error G
1	0	0.0202	0.0203	0.0001+
2	0	0.0236	0.0235	0.0001−
3	0.1	0.0202	0.0199	0.0003−
4	0.1	0.0202	0.0203	0.0001+
5	0.35	0.0151	0.0149	0.0002−
6	0.3	0.0202	0.0201	0.0001−
7	0.1	0.0236	0.0236	0.0000±
8	0.1	0.0236	0.0239	0.0003+
9	0	0.0472	0.0471	0.0001−
10	0	0.0236	0.0234	0.0002−

NEW HAVEN, CONN.

[CONTRIBUTION FROM THE DEPARTMENT OF NUTRITION, OHIO AGRICULTURAL EXPERIMENT STATION.]

THE MODIFIED BENEDICT METHOD FOR THE ESTIMATION OF SULFUR IN FEEDS, FECES AND FOODS.[1]

BY J. O. HALVERSON.

Received July 21, 1919.

In the estimation of total sulfur in solid organic matter, the Wolf and Osterberg procedure[2] of adding fuming nitric acid in the preliminary oxidation and solution of the material (before final and complete oxidation with the Benedict reagent[3]) offers two great difficulties which prevent its general availability for those classes of substances for which the official peroxide method[4] is applicable. First, the use of large amounts (50 to 75 cc.) of fuming nitric acid in Kjeldahl flasks heated over a free flame is tedious, long, and effect solution with difficulty. Second, the high values for blank determinations which are usually obtained when the amount of barium sulfate estimated on the basis of the ordinary charge is relatively small, offer another serious objection.

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[1] An abstract of the work included in this paper was presented at the Cleveland meeting of the American Chemical Society, Sept. 12, 1918.

[2] *Biochem. Z.*, 29, 428 (1910).

[3] The Benedict reagent consists of 200 g. of crystallized copper nitrate, sulfur-free or of known sulfur content, 50 g. of potassium or sodium chlorate and distilled water to make 1000 cc.

[4] Report of the Committee on Editing Tentative and Official Methods of Analysis of the Association of Official Agricultural Chemists, 1915, p. 32.

The length of this process, the constant care and attention required and the large quantities of reagents called for led the writer to investigate the possibility of adapting the Wolf and Osterberg procedure to the above mentioned classes of substances by simplifying the technique of rendering the charge soluble and completing the oxidation with the Benedict reagent without loss by spattering upon ignition; and by reducing to a minimum the values of blank runs on reagents.

The objection to the Wolf and Osterberg procedure on materials which are as difficult to render soluble as feeds and feces has been overcome and the proposed modified method has been in active use during the past year.

It has been shown that concd. nitric acid[1] alone with the Benedict reagent gives low results, probably due to the incomplete oxidation of all sulfur to sulfate. Wolf and Osterberg[2] therefore proposed the use of fuming nitric acid to complete the solution, followed by the Benedict reagent[3] to finish the oxidation. Twenty cc. of fuming nitric acid is added to the material in a 300-cc. round-bottom Kjeldahl flask. The flask is then heated over a small, *free* flame, and additional quantities of acid are added to effect *complete* solution. In practice, however, the charges are as a rule slowly heated over the free flame to dryness with charring, and additional successive portions of fuming acid added with heating until approaching dryness no longer causes charring. The process requires careful and constant attention.

Our adaptation and modification of this tedious and difficult process consists in first softening and disintegrating the material in the flask with 10 to 15 cc. of hot water and allowing it to stand overnight at room temperature, or hot water or steam, the mouth of the flask being closed with a small glass funnel. After 10 hours of digestion, 20 cc. of a mixture[4] of fuming nitric acid and conc. nitric acid (1:4) is added, and the digestion at steam temperature is allowed to proceed continuously, with occasional shaking, for 24 hours.[5] Another portion of 10 or 15 cc. of mixed acid is then added and digestion is continued 15 hours longer until solution is almost complete. Small, resistant, protein-like residues may remain. When continued digestion appears to have no further effect, the solution is transferred in portions to a 60-cc. evaporating dish on the steam bath

[1] *Biochem. Z.*, 9, 307 (1908).

[2] *Loc. cit.*

[3] S. Benedict, *J. Biol. Chem.*, 6, 363 (1909)

[4] Conc. nitric acid containing $^1/_4$ its volume of fuming nitric acid—80 cc. of the latter to 320 cc of conc. nitric acid.

[5] Or two days when steam is off at night.

and the Benedict reagent is added. The complete solution of feeds and feces with fuming nitric acid is not attempted. Almost complete solution is, however, effected with a diluted fuming nitric acid, and oxidation is then completed with the Benedict reagent. Occasionally it is necessary to add a third portion of 10 cc. of the weak fuming acid mixture.

This process does not require close or constant attention. After evaporation to complete dryness, the residues are gradually ignited. The blanks will sputter upon ignition, but this can be prevented by first adding 5 cc. of a 10% sucrose solution, followed by evaporation on the steam bath to complete dryness before heating. Sputtering upon ignition is due to a large excess of the Benedict reagent, in comparison with the amount of organic matter present. On the other hand, too much organic matter in proportion will cause a hard, dry crust to form without fusion. The approximate proportions are given later.

The cause of high blank determinations was found to be due to sulfate in the copper nitrate. The red fuming nitric acid contained none. Various samples of copper nitrate were then tested. One sample from a chemical manufacturer gave a blank of 0.0044 g. barium sulfate per 20 cc. of the Benedict reagent. Almost sulfur-free Benedict reagent was made from Kahlbaum's cupric oxide, pea size, and from Kahlbaum's cupric oxide wire rods, "Zur Analyse."[1] This suggested that sulfur-free copper nitrate[2] may be made from pure sheet copper.

The modified Benedict method as developed by us was checked by the modified official peroxide method of Krieble and Mangum.[3] The latter was first checked by the official peroxide method[4] (see Table I).

The method of Krieble and Mangum was chosen because with it results were more uniform and the limits of variation were narrower. It allows considerable exactness of detail; constant amounts of sodium carbonate and sodium peroxide are weighed out for each determination; the acid used in precipitation of the barium sulfate is 1.6 to 2.1 times the strength recommended by Folin.[5] After precipitation and standing in the cold for two days, the solutions are evaporated to dryness on the steam bath, and the residue is then taken up with 300 cc. of water and 2 cc. of conc. hydrochloric acid. This gives a granular precipitate.

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[1] They contained 0.0009 and 0.0007 g. $BaSO_4$, respectively, per 20 cc. of Benedict reagent; J. T. Baker Chemical Co.'s conc. nitric acid was used.

[2] Later it was found that Baker and Adamson, Easton, Pa., furnish a sulfate-free grade of copper nitrate giving a blank of 0.0008 g. $BaSO_4$ per 20 cc. of the Benedict reagent.

[3] V. K. Krieble and A. W. Mangum Method, personal communication. Also THIS JOURNAL, 41, 1317 (1919).

[4] U. S. Dept. Agr., Bur. of Chem., *Revised Bull.* 107, 23.

[5] Otto Folin, *J. Biochem.*, 1, 147 (1906).

TABLE I

Results by the Official Peroxide and the Modified Peroxide Methods

Sample	Quantity G	$BaSO_4$ Less Blank[1] G	Sulfur G	Sulfur %
	Official Method			
Milk 1403	23.85	0.0525	0.0072	0.030
	23.90	0.0516	0.0071	0.030
	24.28	0.0465	0.0064	0.026
	24.45	0.0490	0.0067	0.028
Av				0.028
	Modified Method			
	25.02	0.0518	0.0071	0.029
	24.90	0.0513	0.0071	0.028
	23.89	0.0469	0.0064	0.027
Av				0.028
	Modified Method			
1404		0.0623	0.0086	0.035
		0.0614	0.0084	0.035
		0.0619	0.0085	0.033
Av				0.034
	Modified Method			
1405		0.0526	0.0072	0.028
		0.0524	0.0072	0.030
		0.0500	0.0069	0.028
Av				0.029

The tendency of the sodium peroxide method to give high results is shown by Wolf and Osterberg[2] who, determining sulfur in 50 to 100 mg. of cystin, found 26.89% which is 0.19% more than formula requires. Furthermore, two samples of feces averaged 0.031 and 0.009% higher than by their modified Benedict method. Schreiber[3] also noted this tendency. One factor causing this in feeds and feces may be silica; this is indicated in Table II, which shows the effect of the precipitation of partly dehydrated silica.

Removal of the silica in feeds and feces gave results in percentages agreeing closely with those by the modified Benedict method to the third decimal place, with an average of 0.003% difference for the modified Benedict method (Table III). The peroxide method without silica removal gave a difference of 0.023% higher. This relation held for feeds (Table III), but this close agreement must not be taken as an indication of the absolute accuracy of the method. The Benedict method checked with an average difference of 3.67%.

The tendency of the peroxide method to give high results due to other causes than the presence of silica is shown by Allen and Johnston,[4] who

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[1] Blank, official method, 0.0019 g.; modified method, 0.0035 g

[2] Wolf and Osterberg, *Loc. cit*

[3] Herman Schreiber, THIS JOURNAL, 32, 977 (1910)

[4] Allen and Johnston, *Ibid.*, 32, 597 (1910)

TABLE II.

Comparison of the Modified Peroxide Method with the Modified Benedict Method, Both Without and With Silica Removed.

	Mod peroxide method			Mod peroxide method with SiO_2 removed compared			
				with the same method without SiO_2 removed		with the mod Benedict method	
Sample	Without SiO_2 removed[1] %	With SiO_2 removed[2] %	Mod Benedict method[3] %	Difference	%	Difference	%
Swine Feces 1502	0.131	0.105	0.105	0.026		0.000	
		0.112	0.110			0.002	
	0.124	0.104	0.113	0.020		0.009	
			0.110				
Av	0.127	0.107	0.110	0.020	18.7	0.003	2.8
Feces 1503	0.126	0.111	0.108	0.015		0.003	
	0.140	0.104	0.111	0.036		0.007	
	0.132	0.108	0.105	0.024		0.003	
			0.104				
Av	0.133	0.108	0.107	0.025	23.1	0.001	0.9

worked on pure solutions, also by Wolf and Osterberg[4] and by Schreiber.[4] In the modified peroxide method the solution of 350 cc (of oxidizing reagent) contained 24 g. NaCl, which with a higher acidity causes a high occlusion as shown by Allen and Johnston. The extent of occlusion of the barium sulfate, however, is determined by running with each set of analyses 3 entirely similar determinations of known amounts of pure potassium sulfate solution approximately equivalent in barium sulfate content to the quantity obtained from the analyses of the organic material itself. The actual sulfate content of an equivalent quantity of the potassium sulfate solution is found by direct precipitation. The difference obtained between these two sets of results gives the values for both occlusion and the sulfate in the reagents. When occlusion is negligible (as indicated by the small quantity of the barium sulfate obtained) the method showed that there was little sulfate present in the reagents. The amount present[5] is, perhaps, due to adsorption and varies with each lot; the average was 0.0046 g. The modified Benedict method gave a blank of 0.0011 g. which was but slightly higher than that found for the determination of sulfur in urine The fuming nitric acid gave a blank of 0.0005 g. for the usual amount taken.

Loss of Barium Sulfate in Filtration and Washing.

Any perceptible precipitate in the filtrate and wash water is, of course, recovered at once. Our experience indicates, however, that slight losses not readily apparent are always experienced,[1] in filtering and washing less than 0.1 g. of barium sulfate precipitate caused by passage of the finer particles of precipitate through the pores of the filter paper, even when paper of such fine texture as Whatman's No. 44 or S. & S. 590 is used with a gravity washing system. These losses were very evident when the filtrates and wash water of an entire set of determinations—all of which looked to be free from precipitates[2]—were combined and allowed to stand covered for 2 to 3 days, for a fine precipitate of

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[1] Less Blank, 0.0070 g. $BaSO_4$

[2] Less Blank, 0.0006 g $BaSO_4$

[3] Less Blank, 0.0001 g. $BaSO_4$

[4] *Loc. cit.*

[5] Blank as determined by Krieble and Mangum, personal communication.

TABLE III

Comparison of the Modified Benedict Method with the Modified Sodium Peroxide Method with Silica Removed

Material and sample No.	Quantity		$BaSO_4$		% sulfur		Comparison of Benedict and peroxide method	
	Peroxide method G.	Benedict method G.	Peroxide method[3] without silica G. av.	Benedict method[4] G. av.	Peroxide method	Benedict method	Difference	%
Ground Corn								
1517	2.7476	2.7476	0.0245	0.0257	0.123	0.129	+0.006	4.9
Linseed Oil Meal								
1518	2.7476	2.7476	0.0802	0.0833	0.401	0.417	0.016	4.0
Wheat Middlings								
1519	2.7476	2.7476	0.0389	0.0403	0.195	0.202	0.007	3.6
General Av.							0.010	4.1
Feces (Swine)								
1502	4.99	3.43	0.0368[5]	0.0274[6]	0.107	0.110	0.003	2.7
1503	3.47	3.44	0.0273	0.0268	0.108	0.107	—0.001	—0.9
1504	4.03	3.45	0.0299	0.0269	0.102	0.107	0.005	4.9
1505	4.07	3.97	0.0301	0.2095	0.102	0.102	0.000	0.0
1506	4.14	3.10	0.0330	0.0230	0.110	0.102	—0.008	—7.3
1507	3.74	3.57	0.0309[7]	0.0302[8]	0.114	0.116	0.002	1.8
1508	4.18	3.23	0.0344	0.0264	0.113	0.112	—0.001	—0.9
1509	3.52	3.35	0.0282	0.0247	0.110	0.101	—0.009	—8.2
1510	4.28	3.45	0.0321	0.0261	0.104	0.104	0.000	0.0
1511	3.58	3.51	0.0262	0.0271	0.101	0.106	+0.005	+5.0
General Av.							0.003	3.17

[1] Excluding dust, etc., this recovery from a large number of determinations averaged 0.0012 g. per determination. A number of more recent results by E. B. Wells, using more care and precautions, reduced this to 0.0003 g. per determination.

[2] The combined filtrates and wash water held up to the direct sunlight showed very fine particles held in suspension.

[3] G. $BaSO_4$ average of 3 determinations, less blank, 0.0040 g. per determination.

[4] Plus loss in filtrate exceeding blank, 0.0006 g. per determination.

[5] Samples 1502–1506 inclusive, less blank 0.0006 g. per determination.

[6] Samples 1502, 1503, less blank, 0.0001 g., Samples 1503–6, less blank, 0.0008 g.; Samples 1502–1506 inclusive, g. $BaSO_4$ average of 4 determinations.

[7] Plus loss in filtrate exceeding blank, 0.0013 g. per determination.

[8] Less blank, 0.0018 g.

barium sulfate settled out. The supernatant liquid was siphoned off, the precipitate filtered and washed, and weighed.

The usual laboratory practice is to discard filtrates and wash water immediately. Recovery of additional precipitate as indicated above shows that the loss may be greater than is here determined, unless unusual care is taken to reduce this loss to a minimum by slow filtering and gentle washing. Furthermore, allowing the precipitated sulfate to stand at room temperature for two days,[1] appears to aid filtration by permitting the particles to grow The formation of a granular barium sulfate precipitate is also assisted by adding the barium chloride hot to the boiling sulfate solution, slowly or by drops. The precipitated solutions are then heated on the steam bath for 3 hours after which they are allowed to stand in the cold for two days Neglect of this precaution will render filtration difficult

Allen and Johnston[2] have shown, contrary to the statements of some chemists, that the presence of potassium chloride does not increase the solubility of barium sulfate In the modified Benedict method, however, approximately 1 g of potassium chloride is used per determination

TABLE IV

Uniformity of Results for Swine Feces Shown by the Modified Benedict Method

Sample No	Quantity G	$BaSO_4$ less blank [3] G	%
1512	2 94	0 0263	0 123
	3 20	0 0281	0 121
	3 73	0 0324	0 119
Av			0 121
1513	2 89	0 0258	0 123
	3 04	0 0285	0 129
	3 37	0 0313	0 128
Av			0 127
1514	4 81	0 0325	0 093
	4 58	0 0310	0 093
	4 52	0 0312	0 095
Av			0 094
1515	4 14	0 0355	0 118
	3 08	0 0256	0 114
	3 97	0 0336	0 116
Av			0 116
1516	2 86	0 0241	0 116
	4 28	0 0364	0 117
	2 79	0 0238	0 117
Av			0 117

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[1] Allen and Johnston recommend 18 hours They state that losses from volatility and occlusion are higher when the precipitate is filtered immediately

[2] THIS JOURNAL, 32, 606 (1910)

[3] Plus loss in filtrate exceeding blank by 0 0011 g per determination

On the other hand, the official peroxide method uses 4 or more g. of sodium chloride per 100 cc. of solution, while the modified peroxide method contained about 13.7 g. per 100 cc.

Comparison of results obtained by the modified Benedict method with those by the modified peroxide method, shows that complete solution of feeds and feces is not necessary, provided that enough Benedict reagent is present to assure complete oxidation. It is, however, desirable to have as complete solution as possible. Table III gives the average results by the modified Benedict method of triplicate determinations obtained on feeds and feces in comparison with those by the peroxide method when silica is removed. The percentages varied in the third decimal place for the modified Benedict method, while in the modified peroxide method a number of results varied in the second place.

Table IV shows the consistency of results obtained by the proposed method. In the hands of another chemist in this laboratory, the method has given as uniform results as are here indicated, but with lower blanks on reagents and less loss in the filtrate.

The Modified Benedict Method.

About 3.44 g. of feces, or 2.7476 g. of feeds[1] is weighed out by difference, placed on half a filter paper, rolled up, and is then put into a 300 cc. Kjeldahl flask. Ten to 15 cc. of hot water is added, the flask rotated occasionally (preferably in the steam bath) to allow any hard lumps to disintegrate and 20 cc. of a mixture of fuming and concentrated nitric acids (1 : 4) is added. The flask is stoppered with a small funnel and allowed to stand for half a day. It is then placed in the steam bath and allowed to digest *slowly* for about 4 days with occasional rotation. At the end of that time another 10 cc. of the acid mixture is added. Digestion is continued until the solution is clear,[2] when it is transferred in portions to a 60-cc. evaporating dish and treated with 20 cc. of the Benedict reagent[3] during evaporation to *thorough dryness* on the steam bath.

Blanks should be run on the reagents. To prevent spattering in heating the blanks, add 5 cc. of a 10% sucrose solution and evaporate to thorough dryness before ignition. The blanks are given the same treatment as outlined above. They should be low in barium sulfate content.

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[1] With this quantity the g. of barium sulfate multiplied by 5 gives the per cent. of sulfur direct.

[2] More resistant residues in feces and feeds may remain, these will not interfere if not present in too great quantity. Small quantities of resistant residues will be taken care of by the Benedict reagent.

[3] Kahlbaum's crystallized copper nitrate was used of which the sulfur content was small. Baker and Adamson's crystallized copper nitrate was found equally low in sulfate.

Procedure in the Benedict Method.

The partly oxidized material in the porcelain dish is evaporated to *dryness*[1] on the steam bath and later baked *slowly* on a gas hot-plate[2] or sand bath. The blackened residue is finally heated until the mass has fused, The heat is then gradually lowered, allowing the fused mass to solidify slowly. The dish when cooled is $^1/_3$ filled with approximately 20 cc. of hot dil. hydrochloric acid (1 : 4) from a wash bottle, and the sides carefully washed down. The dish is then covered with a watch glass and set on the steam bath for 15 minutes.

The perfectly clear solution is then filtered into a 250-cc. beaker, made up to a volume of at least 100 cc., heated to boiling on a hot-plate, and 10 cc. of a boiling 5% barium chloride solution added drop by drop from a calcium chloride tube, the addition consuming about 4 minutes. The covered solution is then placed on the steam bath and allowed to digest for 2 to 3 hours, after which it is allowed to stand in the cold for at least 48 hours, thereby producing a granular precipitate which is readily filtered on No. 590 S. & S. or No. 44 Whatman's filter paper.

By the removal of silica[3] in the sodium peroxide method, this substance was prevented from interfering with the accuracy of the results. In the Benedict method no flocculent silica has been observed in the solution after the barium sulfate has settled. As this solution is not made strongly alkaline or acid, one would not expect silicic acid to be even partly dehydrated or precipitated out.

Advantage of the Modified Benedict Method.

For feeds and feces, results are more uniform[4] than by other methods and the blanks on reagents are consistently low. Occlusion and adsorption appear to be less. There is a complete absence of partly dehydrated silicic acid in the solution after dissolving the fused mass in dilute hydrochloric acid such as is frequently observed in the peroxide method.

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[1] Evaporation to thorough dryness on the steam bath prevents spattering later, on the hot-plate. Beginning ignition of feces on the hot-plate should be gradual. Too much Benedict reagent will cause spattering; too little is indicated, upon ignition, by a hard, dry crust. Too long intense ignition with a large excess of the Benedict reagent will cause excessive etching of the evaporating dishes.

[2] In the baking and ignition processes by this method no evidence of sulfur contamination was obtained when natural gas was used. With coal or water gas, however, the sulfur contamination would be serious unless first removed by passing the gas through an absorbing solution.

[3] Whether any silica comes from the glass container by the action of the strong sodium hydroxide solution has not been determined. Occasional silica in the blanks tends to indicate that this may be one source.

[4] The limits of variation for results on 10 samples of feces by the peroxide method average 1.65 times greater than for the modified Benedict method (Table III). This relation also holds for feeds.

Conclusion.

When silica is present the peroxide method has a tendency to give high results. With removal of the flocculent silica which partly precipitated out, results checked the Benedict method in percentage to the third decimal place. Previously the peroxide method checked to the second decimal place.

The technique of the modified Benedict method has been adapted to facilitate the estimation of sulfur in feeds and feces without requiring undue attention and care. The method of solution of the sample by the Benedict method gives results which check the peroxide method when silica is removed, within an average of 3.17 and 4.17%, respectively, for feces and feeds.

The source of a high value for the blank determination due to sulfate present in the reagents and the need of procuring reagents of sufficient purity for the Benedict method have been pointed out. Not undue quantities of reagents are required for the small amounts of barium sulfate recovered. The modified method is short, the processes are few and require little attention.

The writer acknowledges his obligation to Dr. V. K. Krieble and A. W. Mangum for advice given in the use of their modified sodium peroxide method.

Wooster, Ohio

THE MOLECULAR MECHANISM OF COLLOIDAL BEHAVIOR.

II. THE SWELLING OF FIBRIN IN ALKALIES.

By Richard C. Tolman and Russell S. Bracewell.

Received July 25, 1919.

In a previous article,[1] Tolman and Stearn have studied the swelling of fibrin in acid solutions, and correlated the swelling with the amount of acid adsorbed from the solution. On the basis of their results, they advanced the theory that a piece of fibrin covered with water is a fibrous, spongelike structure with many minute pores or pockets which are themselves full of water. The addition of acid is followed by the adsorption of hydrogen ions to form a double layer on the surface of these pockets with a consequent increase in their size owing to electrostatic repulsion. The addition of a neutral salt to the solution, or the addition of further acid after the limit of adsorption has been reached, is followed by a decrease in swelling, since further ions added arrange themselves, in accordance with well known electrical principles, in such a way as to neutralize the original electrostatic repulsion. The addition of a neutral salt to the solution also leads to further adsorption of acid owing to the fact that the neutralization of the electrostatic forces makes it easier for further hydrogen ions to attach themselves to the walls of the pockets.

[1] This Journal, 40, 264 (1918).

In the present article similar experiments are described which were made with fibrin in alkaline solutions; these have led to similar conclusions as to the molecular mechanism of the swelling produced by alkalies. Owing to the amphoteric nature of its amino acids, fibrin has a tendency to adsorb hydroxide ion from an alkaline solution, just as it adsorbs hydrogen ion from an acid solution, and hence all the phenomena produced by acids can be duplicated with alkalies. The article presents data on the swelling and adsorption in solutions of sodium, potassium and ammonium hydroxides, in mixtures of sodium hydroxide with potassium chloride and potassium sulfate, in sugar and raffinose solutions, and in acetic acid. The work with the sugar and raffinose solutions was performed in order to get an idea as to the adsorption of water itself. The results with acetic acid are presented since they differ from those reported by Tolman and Stearn.

Experimental Methods.

In order that the results of this work should be comparable with those in acid solutions, the procedure previously used[1] was duplicated as nearly as possible, with a few improvements.

Materials.—The blood fibrin[2] was purified by treatment with 0.1 *N* hydrochloric acid and subsequent removal of the acid by continuous washing with distilled water; it was then dried in a current of warm air. Samples of blood fibrin vary as to toughness and resistance to grinding, and a sample having maximum toughness was chosen. Fibrin which does not show this property markedly swells so readily that no supernatant solutions remain for sampling.

The saccharose was the ordinary cane sugar of commerce. The raffinose was an imported sample. The alkalies and salts were ordinary "C. P." reagents.

Measurement of Swelling and Adsorption.

The swelling of the fibrin was measured in special flat bottomed test-tubes using a 0.3 g. sample of the powdered fibrin and 15 cc. of the desired solution. This ratio of materials is the same as that used in the adsorption measurements.

The adsorption experiments were carried out in 250 cc. ground glass-stoppered bottles, using 2 g. of powdered fibrin and 100 cc. of solution. After standing 24 hours, with occasional shaking, the supernatant liquid was drawn off and the alkali titrated with standard acid. If on standing the protein went into solution, as was the tendency in the solutions of alkali of higher concentration, the supernatant liquid was drawn off without shaking. The number of mols of alkali, *A*, adsorbed per g. of fibrin was calculated by the formula

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[1] *Loc. cit.*

[2] Merck's.

$$A = \frac{(C_0 - C)V}{W}$$

where C_0 is the original concentration in mols per liter, C the final concentration after the adsorption has taken place, V the volume in liters of the solution employed, and W the weight of the fibrin in grams.

In the determinations of negative adsorption (adsorption of water) using sugar solutions, a small amount of phenol was added to the solution to prevent bacterial decomposition. The sugar concentrations were measured with a Lippich Large Universal Polariscope. The percentage of sugar may be obtained from the polariscope readings by the well known formula

$$P = \frac{100\,\alpha}{d\,\alpha_0\,l}$$

where α is the rotation, d the density, α_0 the specific rotation and l the length of tube. The number of mols of water, A' adsorbed per g. of fibrin can then evidently be calculated by the formula

$$A' = \frac{(P_2 - P_1)M}{18P_2W} = \frac{(\alpha_2 - \alpha_1)M}{18\alpha_2W}$$

where M is the weight in g. of the solution, P_1 the original concentration, P_2 the final concentration of the sugar, W the weight of fibrin in g., and α_1 and α_2 the original and final rotations.

Experimental Results and Discussion.

Acids.—There is a well known lack of exact reproducibility in experimental results obtained with colloids, owing largely to the great effect which the past history of a colloidal material has upon its immediate behavior. For this reason it seemed desirable as a preliminary to this work to check some of the results of Tolman and Stearn,[1] using the new sample of fibrin. Swelling and adsorption data for the new sample of fibrin were obtained in solutions of hydrochloric acid and nitric acid. The curves obtained were of the same form as those reported by Tolman and Stearn, the adsorption being somewhat higher and the swelling a little less.

With acetic acid, a maximum adsorption of about 0.00095 mol was found at a concentration of about 1.0 N. This differs from the result previously reported in which no maximum was found; this divergence may be due to the great difficulty of obtaining reproducible results in this kind of work. It is felt, however, that the new result is more reliable, particularly because of the use of glass-stoppered bottles in carrying out adsorption experiments instead of finger bowls covered with watch glasses. The new curves for swelling and adsorption are given in Fig. 1, concentrations being plotted as abscissas and swellings or adsorptions per g. of fibrin as ordinates.

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[1] *Loc. cit.*

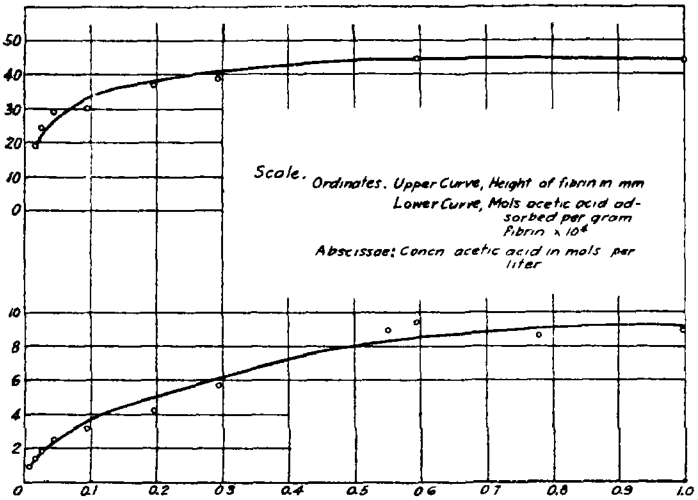

Fig. 1.

Strong Alkalies.—The upper two curves in Fig. 2 show the swelling of fibrin over a range of concentration in solutions of sodium and potassium hydroxides. It is to be noted that the swelling reaches a maximum at a very low concentration and with further increase of concentration

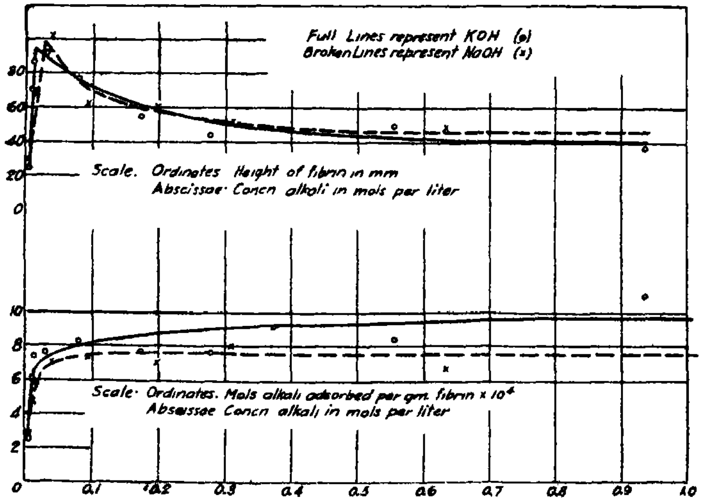

Fig. 2.

there is a reduction in swelling. The two lower curves represent the adsorption of alkali over the same range of concentrations. These are similar to the adsorption and swelling curves obtained in strong acids and may be similarly explained. Increasing the concentration of the alkali, beyond that at which those points on the protein molecule having the greatest affinity for the hydroxyl ions are satisfied, does not result in further adsorption but only increases the ionic concentration of the solution. As long as the number of hydroxyl ions adsorbed increases, the electrostatic forces produced by the adsorbed layer increase. Hence swelling increases as long as adsorption continues. When the maximum adsorption is reached, the further ions added arrange themselves in such a way as to neutralize the electrostatic forces, and subsequent reduction of swelling takes place.

Weak Alkalies.—The upper curve in Fig. 3 shows the swelling of fibrin in ammonium hydroxide up to 0.8 *N*. We note that the swelling gradually increases without reaching a maximum. This curve coincides with the swelling curves for weak acids. On the basis of the theory this is again explained by the fact that with the weak electrolyte there are few ions available for neutralizing the electrostatic field.

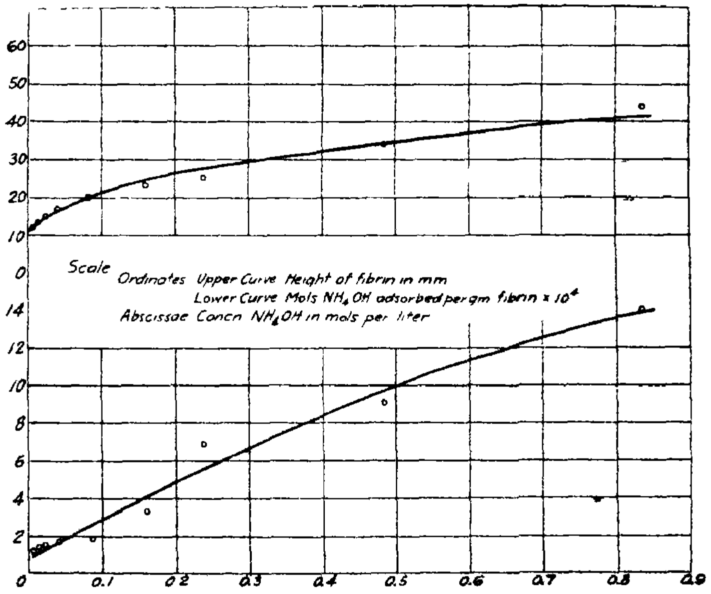

Fig. 3.

The lower curve represents the adsorption of ammonium hydroxide by the fibrin. It is not known whether the wide deviation of some of the points from the curve drawn has any significance or is merely an illustration of the difficulty of obtaining reproducible results in this kind of work. A further set of experiments with ammonia would have been made, except for lack of time and for the exhaustion of the particular sample of fibrin in question. It may be noted that this irregularity occurs with a weak alkali and that a lack of reproducibility in the results obtained in different experiments with a weak acid (acetic) has already been noted. It is felt that the *continued* swelling which is obtained with *weak* acids and *weak* alkalies may cause a breaking down of the fibrin structure which accounts for the variable results.

Mixed Alkalies and Salts.—The effect of additions of potassium chloride and potassium sulfate in reducing the swelling of fibrin in approximately 0.0145 *N* sodium hydroxide solution is shown in the upper two curves of Fig. 4. We see that the addition of a neutral salt produces the same effect in lowering the amount of swelling, as increasing the concentration of the alkali itself beyond the saturation point. This agrees with the results obtained in acid solutions. In any case the controlling factor is the concentration of the free ions which so arrange themselves as to neutralize the original electrostatic repulsion. It is of particular interest to note that mol for mol, potassium sulfate is more effective in reducing the swelling than potassium chloride. This is to be expected because of the greater electrical neutralizing power of a mol of the sulfate over a mol of the chloride.

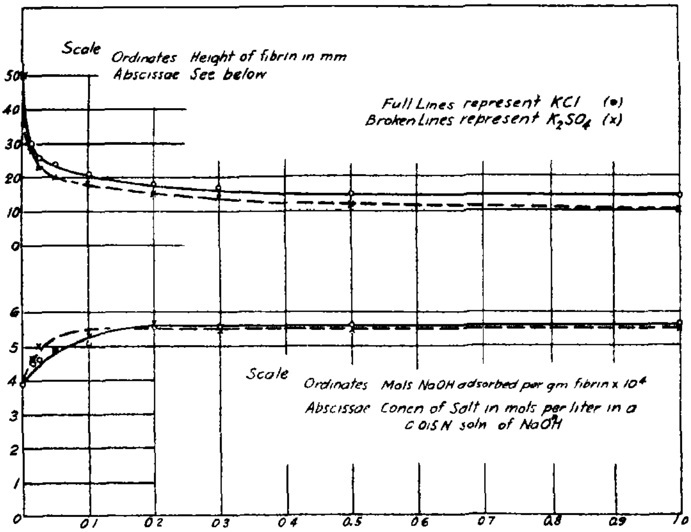

Fig 4

The effect of the neutral salts on the adsorption of hydroxyl ions is also to be noted in the lower two curves of Fig. 4. With solutions 0.0145 *N* with respect to sodium hydroxide the effect of the salt up to a certain concentration is to force the adsorption. This phenomenon, which was also observed in acid solutions, lends additional support to our theory that an electrostatic field is set up by the adsorption of the hydrogen or hydroxyl ions. Such a field would tend to prevent the further adsorption of ions, and if the ions of the neutral salt tend to neutralize this electric field, further adsorption will result. Here again the potassium chloride curve lags behind the potassium sulfate curve. This result is also obviously in accordance with our theory. This effect of the neutral salt is also shown in the curves of Fig. 5 which are similar to the curves of Fig. 4 except that the concentration of sodium hydroxide is 0.134 *N*. We see that the adsorption is forced even beyond the maximum for the higher concentrations of pure strong alkali.

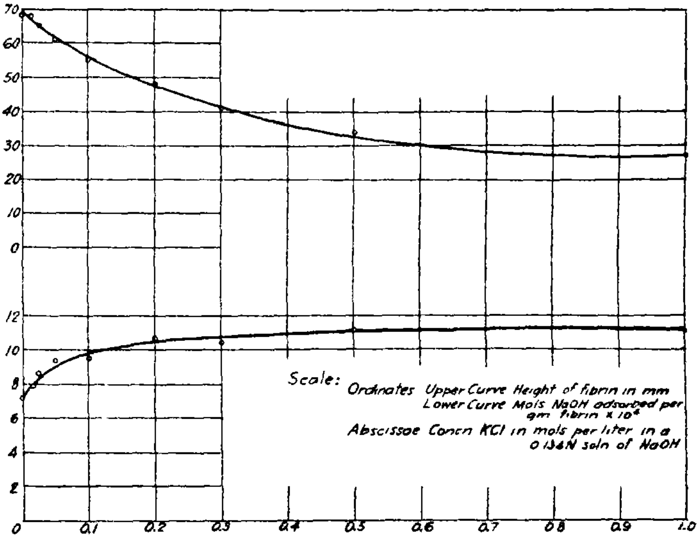

Fig 5

Sugar Solutions.—Tolman and Stearn[1] found that with fibrin in sodium chloride solutions there was an increase in concentration after 24 hours, indicating that there is at least more of a tendency to adsorb water than sodium chloride. In order to try to determine the amount of water actually adsorbed, cane sugar was used as a reference substance; from the measured change of concentration the amount of water adsorbed was calculated. It is to be noted first in the upper curve of Fig. 6 that the sugar solution had no effect on the swelling of the fibrin. In the lower curve where the abscissas give the concentration in mols per liter of saccharose and the ordinates the mols of water adsorbed per gram of fibrin, the adsorption value is noted to have nearly a constant value of about 0.01, a value about 10 times the molal adsorption of acid or alkali per g. fibrin. A small sample of raffinose was available and used for a single measurement at a molal concentration of 0.225; with this reference substance a value of 0.02 mol of water adsorbed per g. of fibrin was obtained.

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[1] *Loc. cit.*

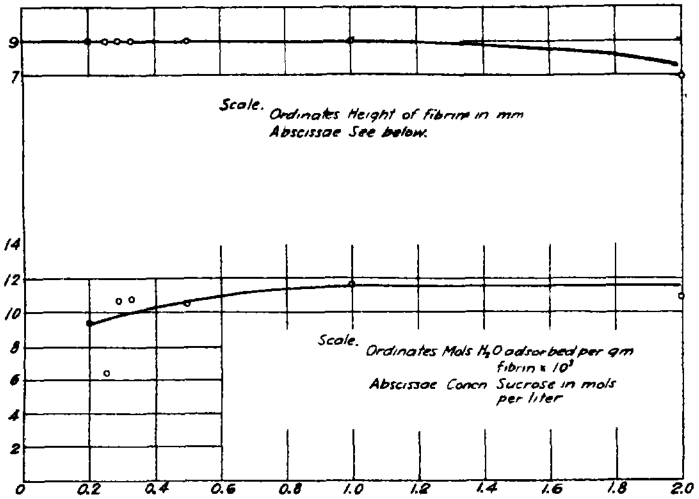

Fig. 6

The evidence indicates that the phenomena is, as would be expected, merely a matter of the relative adsorption of water and the sugars and the results can have no absolute significance. In view of the adsorption of water in sugar solutions we should expect water also to be adsorbed in acid and alkali solutions. Assuming the amount of water adsorbed to be the same as in the cane sugar solution, a simple calculation shows that the amount of water would not affect the concentration of our acids or alkalies appreciably.

Conclusions.

(1) The behavior of fibrin in solutions of strong alkalies and of ammonia, and the behavior on the addition of neutral salts, is similar to the behavior in solutions of strong acids, and can be explained by the theory originally advanced by Tolman and Stearn.

(2) Fibrin adsorbs water from solutions of non-electrolytes.

The work described in this article was performed in the chemical laboratory of the University of Illinois.

WASHINGTON, D. C., and CHICAGO, ILL.

THE MOLECULAR MECHANISM OF COLLOIDAL BEHAVIOR. III. THE CHEMICAL NATURE OF THE ADSORPTION OF ACIDS AND ALKALIES BY THE PROTEIN MOLECULE.

BY RUSSELL S. BRACEWELL.

Received August 1, 1919

In two previous articles[1] the behavior of blood fibrin in acids and alkalies has been studied, and a correlation between the swelling of the fibrin and the adsorption of acid and alkali shown. The purpose of the present article is to discuss the nature of this adsorption process.[2]

The older theories of adsorption assumed that the phenomenon was produced by the action of "physical forces" having somewhat the general character of gravitational attraction. Our newer ideas of adsorption,[3] however, consider the attraction to be more chemical in its nature, arising from stray fields of "chemical force" around atoms whose chemical affinity has not been completely satisfied. On the basis of these newer ideas, we should predict, from the amphoteric chemical nature of the protein molecule, that it would adsorb either hydrogen ion or hydroxide ion, according as to whether the solution is acid or alkaline, and these are found to be the experimental facts, as was shown, for example, in the two previous articles already mentioned. The work cited, moreover, showed not only an adsorption of both acids and alkalies, but also, at least with the strong acids and alkalies, that there is a fairly definite maximum number of equivalents of acid or base adsorbed by the fibrin, which is not markedly increased even by greatly increasing the concentration of the supernatant solution. This affords additional support to the idea that the adsorption process is dependent upon chemical factors and indicates that there may be a limited number of positions on the protein molecule where hydrogen ions or hydroxide ions tend to attach themselves, and that after these positions have been saturated, the protein molecule has become electrically charged to such a degree that further "indiscriminate" adsorption does not take place.

As a matter of fact it appears that the amount of acid "neutralized" by a considerable number of proteins is determined by the number of free amino groups in the molecule. This conclusion differs from that reached by Robertson[4] who, however, based his figures for the number of free amino groups solely upon the criterion that such groups give nitrogen with nitrous acid, whereas the work of Kossel and Cameron[1] indicates that in the case of arginine the amino group in the guanidine nucleus must be regarded as free in spite of the fact that it does not react with nitrous acid. As to the neutralizing power of proteins for alkalies, no definite relation has been found between the amount of base fixed and the structure of the protein molecule. This is in agreement with the conclusions of Osborne, Leavenworth and Brautlecht[2] and of Osborne and Van Slyke[3] that, even in the case of the dicarboxylic acids, glutamic and aspartic, there are no free COOH groups but that these are bound by the free ammonia which is always obtained on the hydrolysis of proteins containing these acids. We may conclude that the adsorption of hydroxide ion by proteins will be of a less specific character.

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[1] Tolman and Stearn, THIS JOURNAL, 40, 264 (1918), Tolman and Bracewell, *Ibid.*, 41, 1503 (1919).

[2] Since writing this article the author has noted the statement by Harkins, Davies, and Clark (THIS JOURNAL, 39, 541 (1917)) that the necessary condition for an adsorption of the kind discussed in the present paper is probably determined by the polar groups in the molecule.

[3] Langmuir, THIS JOURNAL, 40, 1361 (1918).

[4] "The Physical Chemistry of the Proteins," Longmans Green & Co., 1918, p. 20.

Experimental Data.

The following table compares data on the composition of the more common proteins whose amino acid content has been determined by the Van Slyke group method[4] with a fair degree of accuracy, with data on the maximum adsorption of acid by these proteins.

TABLE I

Protein	Total N %	% total N as lysine	% total N as arginine	Free NH_2 groups calculated per g. of protein Equivalents × 10^6	Acid adsorbed per g. of protein Equiv. × 10^6
Fibrin	16.91	11.51	13.86	108	96
Gelatin	17.97	6.32	14.70	85	70
Casein	17.78	10.30	7.41	79	60
Gliaden	17.50	0.75	5.71	23	28
Edestin	18.65	3.86	27.05	115	127

The figures for total nitrogen in these proteins are taken from the work of Van Slyke,[5] for the percentages of this nitrogen combined as lysine and arginine in casein from Van Slyke,[6] and for the other proteins from the work of Matthews.[7] The adsorption data on fibrin, gelatin, gliadin and casein were obtained by titrimetric methods, with phenolphthalein as indicator, using hydrochloric acid over the protein as described in a previous article.[8] The fibrin was also therein described. The gelatin was the commercial high grade slab gelatin. The casein and gliadin were prepared by graduate students in the Laboratory of Physiological

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[1] *Z. physiol. Chem.*, **76**, 457 (1912).

[2] *Am. J. Physiol.*, **23**, 180 (1908–9).

[3] *J. Biol. Chem.*, **22**, 259 (1915).

[4] *Ibid.*, **10**, 15 (1911–12).

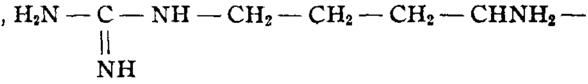
[5] *Loc. cit.*

[6] *J. Biol. Chem.*, **16**, 538 (1915).

[7] "Physiological Chemistry," William Wood & Co., 1916.

[8] Tolman-Bracewell, *Loc. cit.*

Chemistry of the University of Illinois. The acid adsorption data for edestin are taken from Robertson.[1] The adsorption figures, in view of the uncertainty of reproducing colloidal phenomena and of the method of measurement, which involves determining a small change in concentration by difference, are probably subject to an error of something less than 10%. Data by the Van Slyke group method indicates that this method gives results with an error of about 5%.

In these five proteins, lysine and arginine are the only acids with free amino groups, and hence we need only consider these two acids in calculating the "neutralizing power" of these proteins for acid. In the case of lysine, $H_2NCH_2 - CH_2 - CH_2 - CH_2 - CHNH_2 - COOH$, $^1/_2$ of the nitrogen reacts with nitrous acid and hence is assumed to be combined in a free amino group, the other amino group being combined with the carboxyl of another molecule of acid to form the protein chain. In the case of arginine,  $H_2N - \underset{\underset{NH}{\|}}{C} - NH - CH_2 - CH_2 - CH_2 - CHNH_2 -$ COOH, none of the nitrogen reacts with nitrous acid and yet from the structure of the molecule, we may conclude, in agreement with the views of Kossel and Cameron,[2] that the molecule contains one free amino group not bound in the peptide linkage. Proceeding then on the assumption that $^1/_2$ of the lysine nitrogen and $^1/_4$ of the arginine nitrogen is combined in a free amino group, the number of free amino groups per g. of protein has been calculated and is given in the fifth column of Table I. A comparison of these figures with the number of equivalents of acid adsorbed shows reasonable agreement, from which we may conclude that the acid-adsorbing power of proteins is mainly due to the free amino groups present. Similar data were obtained for serum globulin, excelsin, amandin, and legumin, which show the same parallelism, though the divergences are slightly greater, owing probably to the circumstances that the compositions used in the calculations are derived from old methods of analysis and therefore are not well established.

In further support of our theory it may be pointed out that Goto[3] showed that clupein, which contains no lysine, binds approximately one equivalent of sulfuric acid for each molecule of arginine. As another example, Basil and Matula[3] and Pauli and Hirschfeld[3] have given the values 1.65×10^{-2} and 0.85×10^{-2} for the acid adsorbed from 0.05 N hydrochloric acid solution by normal and deaminized gelatin, respectively; the value 1.65×10^{-2} represents the adsorption by the free amino groups in both lysine and arginine, whereas the value 0.85×10^{-2} represents the adsorption by the free amino group in arginine alone since the latter is not deaminized by nitrous acid, and consequently the difference 0.8×10^{-2} represents the combining capacity of the lysine. If we check this against the known composition of gelatin we find that the ratio of $^1/_4$ the arginine nitrogen to $^1/_2$ the lysine nitrogen is 1.2:1, whereas the ratio of the above adsorption values is unity.

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[1] *Loc. cit.*, p. 103.

[2] *Z. physiol. Chem.*, 37, 114 (1902).

[3] *Loc. cit.*

Robertson[1] states that he formerly held the view here presented, that the acid-combining power of a protein is determined by the number of free amino groups, but that in view of more recent work he must conclude that some factor other than the number of free amino groups is responsible for the acid neutralizing power possessed in such a high degree by some proteins. It is believed, however, by the writer, that Robertson has failed to consider the possibility of free amino groups in arginine which do not react with nitrous acid. His statement that 100 equivalents of sturin neutralize no less than 24 equivalents of acid, does not seem unreasonable, when we consider that $^1/_2$ the lysine nitrogen plus $^1/_4$ the arginine nitrogen gives us a figure of 20 equivalents. In considering salmin he concluded that since it gives no nitrogen with nitrous acid, this protein contains no free amino groups; from Kossel and Cameron's work[2] it appears, however, that the amino groups on the guanidine end of the arginine molecule might be free and yet not react with nitrous acid to give nitrogen.

Considering now the positions on the protein molecule most likely to have affinity for the hydroxyl ions we might look to the dicarboxylic acids, but since the COOH groups of glutamic and aspartic acids which are not bound up in the peptide linkage are combined in an amide group with ammonia, it is likely that the affinity at these points would be small. Calculations bear this out in that there is no definite relation between the base adsorbed and the dicarboxylic acid content of the proteins. The effect of dil. alkali in racemizing proteins is of interest in this connection. According to Dakin and Dudley's[3] theory the alkali is the factor in effecting the keto-enol transformation in the peptide linkage which renders the amino acids optically inactive. In such cases it is quite probable that one hydroxyl ion is held at each peptide junction where this transformation occurs. An attempt to correlate alkali adsorption experimental data with their work on racemization was unsuccessful, however, the data are meager and it may be that the method discussed may help in elucidating this question. In general it seems that the proteins having a high affinity for alkalies are high in the simple, straight chained amino acids, but attempts at further correlation failed.[4]

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[1] *Loc. cit.*, p. 20.

[2] *Loc. cit.*

[3] *J. Biol. Chem.*, 15, 271 (1913).

[4] Mr. Bracewell has been good enough to show me the material in his article. I am inclined to agree with him that the amount of acid adsorbed by proteins is de-

The work described in this article was performed in the chemical laboratory of the University of Illinois.

CHICAGO, ILL.

[CONTRIBUTION FROM THE GEOPHYSICAL LABORATORY OF THE CARNEGIE INSTITUTION OF WASHINGTON.]

APPLICATION OF THE THERMIONIC AMPLIFIER TO CONDUCTIVITY MEASUREMENTS.[1]

BY R. E. HALL AND L. H. ADAMS.

Received July 28, 1919

The use of the thermionic amplifier as an aid in making conductivity measurements is an outgrowth of the necessity for accurate work under restricted conditions. We have been confronted with the need of making resistance measurements on saturated solutions of electrolytes in cells whose volume is small and whose electrodes are limited in area to approximately 2 sq. mm. Under these conditions, to avoid heating effects during a measurement, and to minimize polarization at the electrodes, as far as possible, the current through the cell should be made as small as is compatible with a correct bridge setting; and the lower limit to the value of the current is determined by the sensitivity of the telephone.

Ordinarily the conductance cell is designed to meet the requirements of the telephone which is to be used with it. A good telephone has an audibility current of 10^{-8} or 10^{-9} amperes, audibility current being defined as the least current through the telephone which will produce an audible tone. For the majority of uses in connection with measuring conductivities this is sufficient sensitivity. If one is not confronted with limitations in the size and spacing of the cell electrodes, and can work in a quiet room, there is little difficulty in satisfactorily determining the minimum, for one can vary the current passing through the bridge until

termined by their content of the two diamino acids, lysine and arginine. It should not be concluded from this, however, that a protein containing no lysine or arginine would adsorb no acid at all. I believe that, owing to their amphoteric nature, all proteins would adsorb some acid, in the form of a double layer of hydrogen ion and acid ion; the electrostatic force set up by this double layer, however, would discourage further adsorption, and with increasing concentration of acid the adsorption would finally cease to increase. If now, lysine or arginine are present in the protein, the adsorbed acid will be mainly fixed by the strong forces produced by the free amino groups of these acids; after these forces are neutralized, further indiscriminate adsorption at places on the molecule having weaker forces will be prevented by the electrical charge which has been set up. On this basis we should expect the amount of acid adsorbed by ordinary proteins, containing lysine and arginine, to be determined mainly by the content of these diamino acids, as has been found by Mr. Bracewell.

RICHARD C. TOLMAN.

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[1] Presented at the Buffalo meeting of the American Chemical Society, April 7–11, 1919.

it meets the requirements of the telephone. But even then, it is necessary to be very careful in regard to the heating effects caused by the current passing through the cell, and for this reason to follow a rather definite schedule in making bridge settings.[1] Further, increasing the current through the system, as a means of shortening as much as possible the region of absolute silence in making the bridge setting, in addition to increasing the heating effect, is disadvantageous in increasing any errors due to polarization; while decreasing the current to the lowest value compatible with an accurate setting renders the determination of the minimum point a continuous strain on the nerves. Since the dimensions of our conductivity cell were limited by the bomb in which we were working, it was necessary to increase appreciably the sensitivity of the telephone.

Different methods for increasing the sensitivity of the telephone have been discussed by Washburn.[2] (1) Mechanical tuning consists in so adjusting the diaphragm that its fundamental vibration period is the same as that of the current. In the telephones designed for wireless work, or for conductivity measurements, the diaphragm is usually adjusted by the makers to a frequency of about 1000 cycles per second, and for all ordinary work, this frequency is satisfactory. (2) Electrical tuning is said to be of twofold value in that the insertion of capacity in series compensates for the inductance of the telephone and at the same time is effective in damping out higher harmonic tones. Our experience with this type of tuning has been unsatisfactory both with a telephone of low resistance and low impedance, and one in which the resistance and impedance are high. We have found a condenser connected in *parallel* with the telephone to be of advantage, however, in damping out any tones higher than the fundamental. (3) The use of acoustical tuning presupposes a current of almost unvarying frequency, and consequently requires adjustment for any changes in frequency. (4) The use of the stethoscope has been suggested by Curtis[3] as an aid with the telephone. In any of these arrangements, the gain in sensitivity is not great, as the current through the telephone is at best near its allowable lower limit.

The Amplifier.—The thermionic amplifier places at our disposal a means of increasing the current through the telephone almost indefinitely without in any manner changing the current through the remainder of the system, or it allows us to decrease the current through the bridge network very considerably, without any sacrifice in the accuracy of locating the balance position on the bridge.

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[1] Leeds & Northrup Co. *Catalog* 48, p. 29.

[2] THIS JOURNAL, 39, 235 (1917). The original references will be found here.

[3] Mentioned by Taylor and Acree, THIS JOURNAL, 38, 2406 (1916).

Reference to Fig. 1 will make plain the principle[1] upon which the amplifier works. V is an electron-tube generator or audion; it consists of an evacuated bulb containing (1) a heated filament F, which acts as a source of electrons; (2) a metal plate P; (3) a grid of fine wire G, placed between the plate and filament. When the filament is heated, it becomes a source of electrons; with their discharge it acquires a positive charge. Finally this positive charge attains such a value that the electrons are attracted back at a rate equal to their rate of emission, and equilibrium ensues. If, however, the plate P is maintained at a positive potential relative to the filament F, as for instance by the plate battery shown in the figure, the electrons will move from F to P, and a direct current will flow in the plate battery circuit. The amount of this current depends upon the temperature of the filament, the voltage of the battery, and the characteristics of the grid. Fig. 2 illustrates the influence of the grid voltage on the plate current. If the potential of the grid has a sufficiently large negative or positive value, the electronic current is a minimum or maximum, respectively. For a large section of the curve on either side of zero potential, the plate current is a linear function of the impressed voltage. If now an alternating voltage is superimposed on the grid voltage, the current in the plate battery circuit is dependent upon whatever part of the curve we are working in. If the voltage of the grid corresponds to the point A, an increase in

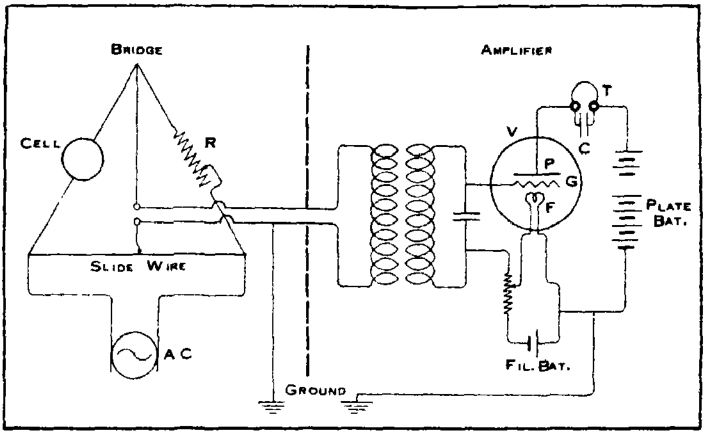

Fig 1.—The Wheatstone bridge and the amplifier. The amplifier is drawn on a considerably larger scale than the bridge.

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[1] L. DeForest, *Electrician*, 73, 842 (1914); *Elec. World*, 65, 465 (1914); I. Langmuir, *Phys. Rev.*, [2] 2, 450 (1913); *Gen. Elec. Rev.*, May, 1915, 327–339; E. H. Armstrong, *Elec. World*, 64, 1149 (1914); H. J. Van der Bijl, *Phys. Rev.*, [2] 12, 171 (1918); M. Latour, *Electrician*, 78, 280 (1916); Bur. Standards, *Circ.* 74, 200 (1918).

negative potential will result in a diminution of current in the plate battery circuit, and a decrease in negative potential will result in a small augmentation of current, but the diminution and augmentation of current will not be equal. On the other hand, at zero potential of the grid, the same decrease and increase of voltage will produce corresponding equal changes in the values of the plate battery current. Oscillographs of the input and plate battery currents taken with the instrument working at this point of the curve, show them to be entirely in phase.[1] For amplification without distortion, then, the grid voltage must correspond to the linear section of the curve. In Fig. 1 it will be seen that the voltage of the grid is controlled by its connection to the negative terminal of the filament battery. Now as the high frequency current from the bridge induces periodic fluctuations of potential in G, the thermionic current between F and P changes simultaneously. Accordingly, the current in the plate battery circuit, and therefore in the telephone T, is periodically increased or decreased, the frequency remaining the same as in the primary current. "It is seen that the device functions broadly as a relay, in that variations in one circuit set up amplified variations in another circuit unilaterally coupled with the former."[2]

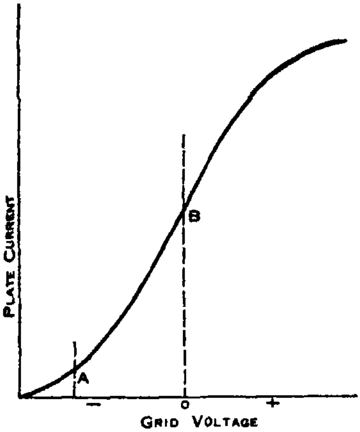

Fig. 2.—The relation of plate current to grid voltage in a 3-element vacuum tube A characteristic curve.

The amplification which is desired determines the number of amplifier bulbs which shall be used. The instrument[3] which we are using (Fig. 3) is a two-step amplifier, manufactured by the Marconi Wireless Telegraph Company and used for wireless telephony in connection with airplane work. It consists of two audion bulbs,[4] connected in cascade, with the necessary transformers and condensers. As shown in Fig. 1, the leads which, in the ordinary conductivity apparatus, connect the telephone to the bridge, are now attached to the input terminals of the amplifier. The telephone may be connected so that either one bulb is used, or the full amplification of the two bulbs obtained. The plate voltage is maintained by a battery of dry cells, and the filament current is furnished by a 6-volt storage battery.

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[1] E. H. Armstrong, *Elec. World*, 64, 1149 (1914).

[2] H. J. van der Bijl, *Loc. cit*

[3] We are indebted to the Radio Laboratory of the Bureau of Standards for the loan of this instrument. It is now possible, with the end of the war, to purchase the instrument in the commercial market.

[4] V. T. 1 tubes, manufactured by the Western Electric Co.

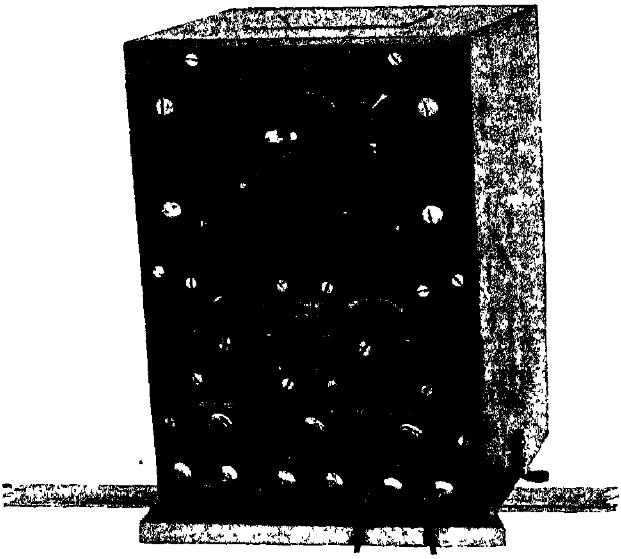

Fig. 3 —The amplifier.

The Gain in Sensitivity by the Introduction of the Amplifier.—The advantage to be gained in conductivity work through the use of the amplifier is shown by the series of measurements recorded in Table I. The current in the bridge circuit, measured by a vacuum thermocouple, was 0.4×10^{-3} ampere, except for one measurement with 0.2×10^{-3} ampere. Metallic, non-inductive resistances were used, and all measurements were made on the ordinary Leeds & Northrup circular slide-wire bridge, with the extension coils in. The figures in the second and third columns of the table represent the number of full divisions on the bridge wire between the points at which the minimum audibility current passes through the telephone; 0.05 division is the smallest unit which can be interpolated. The telephone, a Western Electric instrument, Type CW834, has a direct-current resistance of 2270 ohms. A qualitative determination of the resonance frequency[1] showed it to lie between 900 and 1100 cycles per second. At a frequency of 900 cycles, its effective resistance,[2] as measured in a Rayleigh bridge, is 7500 ohms, and its reactance is 16600 ohms. The telephone was connected to the amplifier so that the amplification from both tubes was obtained.

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[1] A. E. Kennelly and H. A. Affel, *Proc. Am. Acad.*, 51, 421 (1915).

[2] We are indebted to Dr. F. B. Silsbee, of the Bureau of Standards, for making this measurement for us.

TABLE I.

Improvement in audibility obtainable using an amplifier and a 2270 ohm telephone. Frequency: 1000 cycles. Plate battery voltage. 35. Current in bridge circuit. (I) 0.4 × 10^{-3} ampere (II) 0.17 × 10^{-3} ampere

	Resistance in arms of bridge R Ohms	Region of silence on bridge wire in scale divisions		$I_T \times 10^9$ amperes	
		Without amplifier	With amplifier	Without amplifier	With amplifier.
	1000	3	0.05	0.85	0.014
	9500	5	0.05	1.43	0.014
I. ..	30000	6	0.05	1.28	0.011
	60000	10	0.40	1.46	0.058
II	30000	24	0.40	2.18	0.036
			Average,	1.44	0.027

The audibility current of a telephone according to Washburn[1] is given by the equation

$$I_T = \frac{\Delta R_B R I}{\left(\frac{R_B}{2} + R\right)\left(\frac{R_B}{4} + \frac{R}{2} + R_T\right)} \qquad (1)$$

in which I_T is the current through the telephone I, that in the circuit, ΔR_B is one-half of the resistance of the section of wire ("region of silence") given in the table, R_B the resistance of the slide wire, R the resistance in the arms of the bridge, and R_T the effective resistance of the telephone. The expression $\left(\frac{R_B}{4} + \frac{R}{2} + R_T\right)$ represents the resistance of the telephone circuit; no term appears for the reactance, as this has presumably been eliminated by the insertion in series with the telephone of the proper capacity. If, however, the circuit has not been tuned to resonance in this way, its impedance will be given by the expression $\sqrt{\left(\frac{R_B}{4} + \frac{R}{2} + R_T\right)^2 + (L\omega)^2}$, in which $L\omega$ represents the reactance of the telephone at the frequency at which R_T was measured; and our equation for I_T becomes

$$I_T = \frac{\Delta R_B R I}{\left(\frac{R_B}{2} + R\right)\sqrt{\left(\frac{R_B}{4} + \frac{R}{2} + R_T\right)^2 + (L\omega)^2}} \qquad (2)$$

With a telephone of low resistance and inductance, the use of either equation will give practically identical values for I_T; but if the resistance and inductance are high, as in our telephone, and the circuit is not tuned to resonance, the latter equation should be used.

Equation 2 has been used in making the calculations for the table. The average value of I_T, when no amplifier was used, is seen to be 1.44 × 10^{-9}; with the amplifier, it becomes 0.027 × 10^{-9}, *i. e.*, the telephone becomes apparently 50 times as sensitive. Of course, in the latter case, I_T does not represent the real current through the telephone, but is a measure of the effective sensitivity of telephone and amplifier combined. In other words, a current no greater than $0\ 027 \times 10^{-9}$ ampere would produce an audible tone in a telephone whose sensitivity was equal to that of telephone and amplifier combined. It is readily seen that the introduction of the amplifier permits the current through the bridge to be reduced to $^1/_{50}$ of the value necessary when no amplifier is used, with no loss in accuracy in determining the null setting; or a reduction of the current to perhaps $^1/_{10}$ of its value, while still retaining the sensitivity of the telephone at several times the value it had without the amplifier.

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[1] THIS JOURNAL, 38, 2431 (1916), 39, 235 (1917).

It will be noted that the telephone used in these tests was a high resistance instrument. This should be the case for use with the amplifier, as it develops the greatest power when working into a resistance of several thousand ohms. However, tests were made on several other telephones of varying resistance, the results of which are shown in Table II. It will be seen that in every case, with constant current, the use of the amplifier has greatly diminished the region of silence on the bridge wire. If I_T is calculated as in the preceding table,[1] every telephone tested with the amplifier shows an audibility current value of less than 1×10^{-9} amperes; in fact, very much less except in one instrument. The high resistance telephone of the Western Electric Co., developed especially for work in wireless telegraphy and telephony, is decidedly the most sensitive. On the whole, this type of test is quite unsatisfactory, but serves to determine the relative sensitivity of the telephones. The measurements show that with the insertion of the

TABLE II

Comparison of several telephones with and without the amplifier

Frequency 1000 cycles Plate battery voltage 35 Current in bridge circuit: $0\ 33 \times 10^{-3}$ amperes $R = 10{,}000$

Telephone	Resistance of telephone	Division of bridge wire for audibility current: Without amplifier	Division of bridge wire for audibility current: With amplifier	$I_T \times 10^9$: Without amplifier	$I_T \times 10^9$: With amplifier.
1 Western electric CW834	2270	4 0	0 05	0 94	0 012
2 C Brandes	1052	10 0	0 25	7 70	0 19
3 Unknown make	154	35 0	0 4	31 60	0 35
4 Western electric tunable	106	100 0	1 0	91 00	0 91
5 Ordinary Bell . . .	88	7 0	0 25	6 40	0 23
6 Unknown make	63	60 0	0 5	55 00	0 46

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[1] With this difference, that with the exception of No 1, which was calculated by Equation 2, the direct current resistance was used for R_T, and the reactances were not taken into consideration. This will affect the results but little except in No. 2, in which the audibility current would be smaller, undoubtedly, if the impedance were used.

amplifier, even a relatively poor telephone becomes more sensitive than the very best telephone without it.

With the introduction into the circuit of an instrument as sensitive to all electro-magnetic disturbances in the vicinity as the amplifier is, naturally much care must be taken. If there are any appreciable inductive effects nearby, caused, for example, by electric furnaces fed by alternating current, a tone will be heard in the telephone whose pitch corresponds to the number of cycles of the a. c. supply, or the harmonics of this. The click of the relay attached to the thermostat, and any sparking in the generator of the high frequency current, will be heard. The latter, of course, would be eliminated entirely if the Vreeland oscillator were used as a source of current. However, using a Holtzer-Cabot generator, we have had but little trouble from the accidental sounds arising from this source. A good ground connection both to the bridge and to the amplifier is necessary, and the various cables leading to the bridge should be armored and this armor grounded. Our bridge, on account of the shop and power plant noises nearby, had been placed in a telephone booth. When the amplifier was placed in the booth, its proximity to the other parts of the bridge and to the operator was such that the null setting obtained could not be depended upon to give the true resistance. When it was placed outside the booth, and shielded,[1] this difficulty disappeared entirely, so that measurements of metallic resistances made with direct and alternating current have checked repeatedly to 1 part in 50 to 80 thousand. A condenser in parallel with the telephone is advantageous in damping out any harmonics. It is necessary further to adjust very carefully by the usual air condenser the capacity in the arm containing the Curtis coils, especially in the case of saturated solutions in small cells such as we are using. By proper adjustment of this capacity, however, and that in the telephone circuit, a minimum is obtained which is entirely devoid of either the higher notes or the fundamental.

The current[2] through the telephone, when used with an amplifier, consists (1) of the direct current maintained by the plate battery when no alternating voltage is applied to the grid; (2) of the alternating current which is present when such voltage is applied; (3) of a first harmonic; and (4) of a d. c. component due to the alternating input voltage. The only current of importance in amplification is the alternating output current, and this is a linear function of the voltage impressed upon the input circuit. The power amplification is independent of the input and the frequency. When the amplifier works into an impedance equal to or greater than its own, the harmonic becomes negligibly small as compared to the main alternating current. The rapid increase in current through the telephone circuit as the sliding contact moves away from the null position on either side, and the consequent large increase in the sound from the telephone render the determination of the minimum setting very sharp, so that in work in which a minimum setting may be made readily with the ordinary arrangement, the introduction of the amplifier is a source of much satisfaction, owing to the very rapid decrease of sound to entire silence as the sliding contact passes over the balance point.

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[1] Placing the amplifier in a grounded metal can proved to be a convenient and effective method of shielding.

[2] H. J. Van der Bijl, *Loc. cit.*

Our work necessitates measuring resistances of saturated solutions in a cell whose maximum external diameter is 13 mm., and whose electrodes may be separated by no more than 55 mm. Further, the restricted portion of the cell must be of large enough diameter to allow free circulation of the solution. If we allow 5 mm. for the diameter of this portion of the cell, the resistance for a saturated sodium chloride solution is about 100 ohms. The measurements should not differ among themselves by more than 0.003%. The small size of the electrodes necessitates considerable care to eliminate the effects of polarization. The possibility therefore, of greatly reducing the current, without decreasing the accuracy of determining the position of silence on the bridge wire, has been of great value to us. We are working, too, in a room in which the installation of a telephone booth has not sufficed entirely to remove distracting sounds. But the introduction of the amplifier has made the determination of the minimum an easy matter even under these adverse conditions.

The Electron Tube as a Source of Alternating Current.—By means of an arrangement[1] such as that shown in Fig. 4, the electron tube becomes a generator of high frequency current. The frequency is controlled by the condensers C and C′, one of which is of small capacity, and continuously variable over its range; the other, variable in steps of perhaps 0.005 microfarad. A generator of this gen-

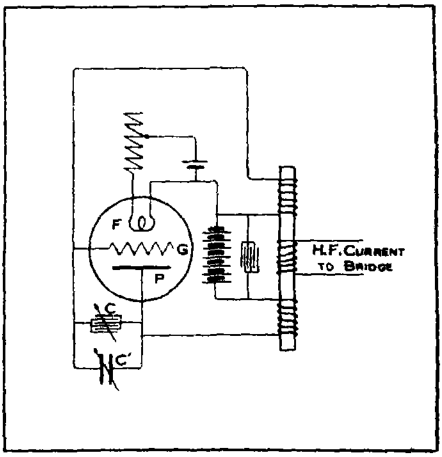

Fig. 4.—The electron tube as a generator of alternating current.

[1] This arrangement was brought to our attention by Dr. J. M. Miller, of the Radio Laboratory, Bureau of Standards.

eral type may be made to yield a current of from a few tenths of a milliampere or less to 25 amperes, and with a frequency varying from $^1/_2$ cycle per second to 50 million cycles per second[1]

As a current generator for the preceding measurements, we used as oscillator a V.T. 1 tube, of the same type as used in the amplifier. The plate voltage was maintained by a 56-volt storage battery; the current for the filament was taken from the same source. The transformer was one which we happened to have; the resistance of the primary coils was 205 ohms, their inductance 25 henrys; the resistance of the secondary coils was 0.76 ohm, the inductance 0.064 henry. While the limits of frequency were not determined, a variation from a very few cycles per second to the limit of the ear for detection, was readily obtained by varying the capacities C and C′. For work at 1000 cycles, C and C′ could be omitted entirely, merely varying the current through the filament giving a sufficient range of frequency.

Table III contains data showing the current at a frequency of 1000 cycles in the external circuit when its total resistance was varied from 19000 to 550 ohms. The available power, although only a small fraction of a watt, would often prove sufficient for conductivity work. Of course, much more power could be obtained with a larger tube or higher plate voltage.

TABLE III

Current obtainable from a V. T. 1 tube acting as generator, with varying external resistance

Plate voltage. 56. C and C′. Set at 0

Transformer	Resistance ohms	Inductance henrys
Primary.......	204.8	25.4
Secondary.....	0.76	0.064

Total external resistance	Vacuum thermocouple: microvolts	Current milliamperes	Power watts
19200	41	0.33	0.0021
14200	72	0.44	0.0027
9200	154	0.64	0.0038
4850	547	1.26	0.0077
2700	1630	2.2	0.0131
1600	3110	3.1	0.0154
1000	5200	4.2	0.0176
800	6230	4.7	0.0177
700	6820	4.9	0.0168
600	7670	5.4	0.0175
550	8210	5.6	0.0173

The use of an electron tube as a source of alternating current in resistance measurements makes available a generator at once cheap and providing a wide range of frequency. Its main disadvantage lies in the fact that a first harmonic is present, which is particularly noticeable at low frequencies; at 1000 cycles or more, it is not noticeable enough to be troublesome.

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[1] W. C. White, *Gen. Elec Rev*, 1916, 771 (September); 1917, 635 (August).

Conductivity Measurements at Extreme Frequencies.—One other point of value in the application of the amplifier to conductivity measurements may be mentioned here. In wireless work, in which undamped oscillations of high frequency are used, the pitch of the resulting notes may be too high to be audible but the signals can be made audible in a telephone by beats. For instance, if two sources of oscillations, one of a frequency of 100,000 and the other of 101,000, act together on the same circuit, the note heard in the telephone will be that due to 1000 pulses per second. In wireless the one source of oscillations is the antenna, receiving them from the sending station; the other source is the electron tube itself, so adjusted to act as an oscillator. In this way, the tube acts simultaneously as a local source of oscillations, and as a receiver and amplifier of oscillations from the sending station. This is called the autodyne method. If, then, it would be advantageous for any reason to use higher frequencies than 5 or 10 thousand cycles in making conductance measurements, by an application of this method, the telephone could still be used for determining the point of balance in the bridge. We are planning to investigate this use of the audion tube.

Summary.

1. The use of an amplifier in conjunction with the telephone in the measurement of the resistance of solutions makes much simpler the determination of the balance position of the bridge. Any ordinary telephone becomes a more sensitive instrument with the amplifier than the best telephones without it. When a sensitive telephone is used, the current through the bridge may be reduced to a tenth of the value necessary without the amplifier, and the instrument still will have several times the sensitivity it has without the amplifier.

2. An electron tube may be used as a source of alternating current for conductance measurements. Its advantages are its cheapness and the wide range of frequencies which may be obtained with it. A first harmonic is present in the current, which is noticeable at low frequencies, but which is not troublesome at a frequency of 1000 cycles or more.

3. If, for any reason, it should be desired to use frequencies in conductance measurements beyond the limit of the human ear, a telephone could still be employed to indicate the bridge balance by the use of the autodyne method.

WASHINGTON, D. C.

[CONTRIBUTION FROM THE OFFICE OF PLANT PHYSIOLOGICAL AND FERMENTATION INVESTIGATIONS, BUREAU OF PLANT INDUSTRY, U. S. DEPARTMENT OF AGRICULTURE.]

THE CAUSE OF AND REMEDY FOR CERTAIN INACCURACIES IN HAUSMANN'S NITROGEN DISTRIBUTION METHOD.

BY S. L. JODIDI[1] AND S. C. MOULTON.

Received July 29, 1919.

The importance of proteins as life carriers in the plant and animal organism, as well as the significance of amino acids as simple substances out of which the protein molecule is built up, has long been recognized. The amino acids, along with the proteins assume added significance because of their importance in nutrition, as demonstrated by the more recent researches of Osborne[2] and Mendel, McCollum,[3] Van Slyke,[4] Hart,[5] Abderhalden[6] and their collaborators. It is for this reason that it is frequently desirable to analyze for the amino acids quantitatively. This can be accomplished by estimating the chemical groups characteristic of the different amino acids, according to the well-known method of Van Slyke,[7] or the diamino acids may be isolated and determined according to the method of Kossel[8] and Kutscher[9] and their collaborators, while the monoamino acids may be estimated according to Fischer's ester method.[10]

Whereas Van Slyke's method has the great advantage that it yields quantitative results with but a small amount of material (about 3 g. of protein) its disadvantage is that the time factor is not insignificant. On the other hand, analysis of proteins by the methods of Kossell and Kutscher and those of Fischer requires very much more material and time.

It is true that by Hausmann's method[11] the nitrogen distribution in the protein molecule can be determined in a very short time and with but one g. of protein material. But although the method yields fairly accurate results for acid amide nitrogen, the results for diamino and monoamino acid nitrogen are far from being accurate. Osborne and Harris[12] have essentially improved Hausmann's method by showing how to determine humin nitrogen (which was not done by Hausmann) and by elaborating the exact conditions under which the diamino acids can be precipitated quantitatively. They also suggested calculating monoamino acids by difference rather than estimating them directly, since their direct determination by the Kjeldahl method, in the presence of a large quantity of phosphotungstic acid incidental to Hausmann's method, yields too low results.

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[1] We wish to express our thanks to Mr. K. S. Markley for some assistance in this work.

[2] *J. Biol. Chem.*, 12, 473 (1912), 13, 233 (1912); 17, 325 (1914); 18, 1 (1914); 20, 351 (1915), 26, 1, 293 (1916); 29, 69 (1917).

[3] *Ibid.*, 19, 323 (1914); 20, 415 (1915); 28, 211, 483 (1916).

[4] *Ber.*, 43, 3170 (1910), *J. Biol. Chem.*, 16, 231 (1913).

[5] *J. Biol. Chem.*, 21, 239 (1915); 26, 457 (1916); 29, 57 (1917); 31, 415, 445 (1917).

[6] *Z. physiol. Chem.*, 96, 1 (1915).

[7] *J. Biol. Chem.*, 10, 15 (1911–1912); 22, 281 (1915); 23, 411 (1915).

[8] *Z. physiol. Chem.*, 31, 165 (1900–01).

[9] *Ibid.*, 49, 318 (1906); 52, 108 (1907).

[10] *Ibid.*, 33, 151, 412 (1901).

[11] *Ibid.*, 27, 95 (1899); 29, 47, 136 (1900).

[12] THIS JOURNAL, 25, 323 (1903).

In applying Hausmann's method on various occasions, the writer[1] found that while the figures for acid amide nitrogen were on the whole uniform and fairly accurate, those for diamino and monoamino nitrogen were not as uniform and sometimes could not be duplicated. Observations on Hausmann's method show that the more magnesium oxide is used in the distillation of the acid amide nitrogen, the more humin nitrogen is retained by the magnesium oxide. This is plainly visible, since the color of the residual liquid containing the basic and non-basic nitrogen is lighter when a larger amount of magnesium oxide is used. In this connection Hausmann[2] fails to specify the amount of magnesium oxide to be added to the evaporated hydrolyzed substance, while Osborne and Harris[3] recommend adding this reagent until it is in slight but distinct excess. However, because of the insignificant solubility of magnesium oxide in water (1 : 55368) and the slight alkalinity of its solution one is apt to use a considerable excess. This is especially true in the analysis of biological materials containing chiefly carbohydrates and but a small proportion of proteins and amino acids. Excessive use of magnesium oxide, however, involves significant errors, as will be shown in the experimental part of this paper.

Experimental.

Casein.—The casein used in these experiments was prepared from skim milk essentially according to the method of Hoppe-Seyler.[4] The purified, air-dried casein, contained 8.89% of moisture and 15.53% of nitrogen, calculated to the oven-dried substance. 1.2 g. quantities of air-dried casein were treated with 75 cc. of 20% hydrochloric acid and kept boiling under reflux for 10 hours. Each of the hydrolyzed portions was next evaporated on the steam bath, practically to dryness, transferred quantitatively to 800-cc. Kjeldahl flasks with 250 cc. of boiling hot water, cooled and distilled with various amounts of magnesium oxide previously mixed to a cream with 100 cc. of water. The distillate was titrated with 0.1 *N* sulfuric acid, in order to determine the acid amide nitrogen.

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[1] S. L. Jodidi, THIS JOURNAL, 32, 396 (1910); 33, 1226 (1911); 34, 94 (1912); also Mich. Agr. Expt. Sta., *Tech. Bull.* 4 (1909); Jodidi and Wells, Iowa Agr. Expt. Sta., *Research Bull.* 3 (1911); Jodidi, Kellogg and True, *J. Agr. Research*, 15, 385 (1918).

[2] *Z. physiol. Chem.*, 27, 98 (1899).

[3] THIS JOURNAL, 25, 331 (1903).

[4] Hoppe-Seyler's *Handbuch d. Physiol. u. Pathol. Chem. Anal.*, Berlin, 1909, p. 488.

The magnesium oxide residue was now filtered off and thoroughly washed with boiling hot, ammonia-free water until free from hydrochloric acid. The filter and its contents were next put into a 500-cc. Kjeldahl flask, to which the residue in the 800 cc. flask was then quantitatively transferred by means of dil. sulfuric acid, and the whole analyzed by the Kjeldahl method, to obtain the proportion of "humin" nitrogen.

Filtrate and washings from the magnesium oxide residue were evaporated on the water bath to 100 cc., cooled to 20°, and treated with 5 g. of sulfuric acid and 30 cc. of a solution containing 5 g. of sulfuric acid and 20 g. of phosphotungstic acid per 100 cc. After about 24 hours the precipitate was filtered out and washed with a solution containing 5 g. of sulfuric acid and 2.5 g. of phosphotungstic acid per 100 cc. The washed precipitate and the filter were subjected to oxidation for 8 hours, according to the Kjeldahl method, which gave the nitrogen of diamino acids.

In all experiments a correction was made for the nitrogen present in the reagents.

The proportion of the monoamino acid nitrogen was found by subtracting from 100 the sum of the nitrogen per cents. obtained by the above operations.

The results representing the average of duplicate estimations are presented in Table I. Examination of the table shows that the percentage of the acid amide nitrogen is practically the same in all experiments, but that the percentage of nitrogen contained in the magnesium oxide precipitate is higher when a larger quantity of magnesium oxide is used for distillation, and the percentages of monoamino and diamino nitrogen are correspondingly lower. Since the hydrolysis of the various portions of casein took place under identical conditions, the amount of humin nitrogen formed should be the same in all cases. Hence, the fact that different quantities of nitrogen were retained by the magnesium oxide clearly indicates that diamino and monoamino acid nitrogen as well as humin, nitrogen, were adsorbed.

TABLE I.—NITROGEN DISTRIBUTION IN CASEIN.

Magnesium oxide used for distillation. G.	Nitrogen of acid amides.		Nitrogen of magnesium oxide ppt.		Nitrogen of diamino acids.		Nitrogen of monoamino acids.	
	Oven-dried casein. %.	Casein nitrogen. %.	Oven-dried casein. %.	Casein nitrogen. %.	Oven-dried casein. %.	Casein nitrogen. %.	Oven-dried casein. %.	Casein nitrogen. %.
4.0	1.60	10.28	0.74	4.78	2.79	17.97	10.38	66.84
2.0	1.59	10.21	0.41	2.60	2.96	19.03	10.59	68.17
1.0	1.58	10.15	0.27	1.72	...	...	...	...
0.5	1.59	10.22	0.20	1.30	3.27	21.05	10.47	67.43

If the humin nitrogen formed in the course of the casein hydrolysis were insoluble it should be possible to separate and estimate its exact proportion; and the nitrogen present in the magnesium oxide would be simply adsorbed nitrogen of diamino and monoamino acids. To determine what actually happens, several more portions of 1 2 g. of air-dried casein[1] were hydrolyzed under exactly the same conditions as before. The hydrolyzed liquids, however, were evaporated on the water bath to dryness, taken up with hot water, filtered through a double filter and refiltered until the filtrate was perfectly clear. The black residue on the filter was then washed with boiling hot ammonia-free water until the filtrate was free from chlorine, whereupon the filter and residue were oxidized by the Kjeldahl method and the proportion of the insoluble humin nitrogen thus determined. The dark brown but perfectly clear filtrate and washings from the insoluble black residue were concentrated and used for distilling off, with the aid of magnesium oxide, the ammonia corresponding to the acid amides, etc., as already outlined. The data in question which represent the average of duplicate analyses are summarized in Table II.

TABLE II —NITROGEN DISTRIBUTION IN CASEIN, WITH REMOVAL OF THE INSOLUBLE HUMIN NITROGEN

Magnesium oxide used for distillation G	Insoluble humin nitrogen		Nitrogen of acid amides		Nitrogen in magnesium oxide ppt		Nitrogen of diamino acids		Nitrogen of monoamino acids.	
	Oven dried casein %	Casein nitrogen %	Oven-dried casein %	Casein nitrogen %	Oven-dried casein %	Casein nitrogen %	Oven dried casein %	Casein nitrogen %	Oven-dried casein. %	Casein nitrogen. %.
4 0	0 03	0 18	1 58	10 26	0 77	4 96	2 95	19 16	10 07	65 46
2 0	0 02	0 11	1 57	10 22	0 32	2 06	3 07	19 93	10 42	67 68
1 0	0 01	0 08	1 61	10 46	0 23	1 48	3 29	21 38	10 25	66 60
0 5	0 02	0 16	1 59	10 32	0 11	0 72				...
Results of Osborne and Harris[2] .			1 61		0 21		3 49		10 31	
Results of Hausmann[3]			2 13				1 75		12 06	.
			2 07				1 61		11 81	
							1 52			..
							2 33			..
							2 00	.	.	.
			2 10	(Ave)			1 84	(Ave.)	11 93	(Ave.)

In glancing over this table it is readily seen that the proportion of insoluble humin nitrogen is insignificant, the data for acid amide, diamino and monoamino nitrogen fully corroborating the results already reported in Table I. While the successive treatment of the magnesium oxide precipitate with additional and larger quantities of water influences somewhat the relative amounts of nitrogen remaining in it and in the filtrate this influence is not considered great enough to affect the conclusions drawn.

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[1] This casein had a moisture and nitrogen content slightly different from the casein used in the experiments already reported

[2] THIS JOURNAL, 25, 349 (1903).

[3] *Z. physiol. Chem.*, 27, 103–4 (1899).

When we compare those samples in Tables I and II, in which one g. of magnesium oxide was used for distillation, we find that these results agree very well with those of Osborne and Harris.

Hausmann's results differ considerably from those of Osborne and Harris, while ours are between the two. It is interesting that Hausmann obtained concordant duplicates in the estimation of acid amide nitrogen, while his figures for diamino nitrogen show considerable variations. In the light of the results in Tables I and II, it seems safe to assume that the considerable fluctuations in the diamino nitrogen obtained by Hausmann may have been due to different amounts of magnesium oxide used in the distillation, in addition to the fact that Hausmann did not quite succeed in rendering the conditions for the precipitation of diamino acids strictly quantitative.

Similar experiments carried out with egg albumin and gelatin[1] have led essentially to the same conclusions. The proportion of nitrogen found in the magnesium oxide precipitate was higher, and that of diamino and monoamino nitrogen was correspondingly lower, the more magnesium oxide was used for distillation, the amount of the latter being of no influence on the proportion of acid amide nitrogen.

Spinach.—In previous work[2] it was ascertained that the nitrogen of the spinach plant (*Spinacia oleracea*) is made up of proteins, and nonproteins (acids, amides, amino acids, etc.). For the following experiment we used air-dried, powdered leaves[3] from healthy spinach plants collected on the Childreth farm near Norfolk, Virginia. Several 5 g. portions were transferred to round bottom flasks to which 250 cc. of 20% hydrochloric acid was added and kept boiling under a reflux condenser for 10 hours. The contents of the flask were now filtered on a Büchner funnel provided with a cloth filter and washed with boiling hot, ammonia-free water until the filtrate was free from chlorine. The filtrate and washings were, on cooling, made up to a definite volume and shaken thoroughly. Several 500 cc. quantities of this solution, each containing 216.2 mg. of nitrogen, were now evaporated on the water bath to dryness, whereupon the separation of the acid amide, diamino nitrogen, etc., was effected as with casein. The results which are recorded in Table III

[1] The data in question may be omitted here for the reason that the egg albumin and gelatin used were not quite pure.

[2] Jodidi, Kellogg and True, *J. Agr. Research*, **15**, 393 (1918).

[3] The analysis showed them to contain 7.62% moisture and 5.00% nitrogen, calculated to the oven-dried substance.

fully corroborate the conclusions drawn from the experiments with casein, ovalbumin and gelatin.

TABLE III.—NITROGEN DISTRIBUTION IN SPINACH

Magnesium oxide used for distillation G	Nitrogen of acid amides		Nitrogen in magnesium oxide ppt		Basic nitrogen		Non basic nitrogen	
	Oven-dried Spinach %	Spinach nitrogen %	Oven dried Spinach %	Spinach nitrogen %	Oven-dried Spinach %	Spinach nitrogen %	Oven dried Spinach %	Spinach nitrogen %
4.0	0.88	17.61	0.26	5.28	0.79	15.81	3.06	61.30
2.0	0.89	17.77	0.19	3.77	0.81	16.22	3.11	62.24
1.0	0.88	17.68	0.11	2.13	0.85	16.98	3.16	63.21

An attempt to distill the evaporated hydrolyzed spinach with 0.5 g. of magnesia was unsuccessful, the amount of the latter being insufficient to render the substance alkaline.

Summary.

1. The proportion of acid amide nitrogen obtained by Hausmann's method, as modified by Osborne and Harris, is constant and does not depend upon the quantity of magnesium oxide applied to the distillation.

2. The percentage of nitrogen contained in the magnesium oxide precipitate is the higher, the greater the quantity of magnesium oxide employed in distillation.

3. Conversely, the proportion of monoamino and diamino nitrogen is the smaller, the larger the amount of magnesium oxide used in distillation.

4. In order to obtain uniform results and a minimum of "humin" nitrogen it is necessary to use the least possible amount of magnesia which is sufficient to render the substance to be distilled alkaline. In the case of plant and animal materials the uniform application of one g. of magnesium oxide seems to be satisfactory, while in the case of proteins 0.5 g. suffices.

WASHINGTON, D. C.

[CONTRIBUTION FROM THE GEOPHYSICAL LABORATORY OF THE CARNEGIE INSTITUTION OF WASHINGTON.]

THE HYDROCHLORIC ACID COLOR METHOD FOR DETERMINING IRON.

BY J. C. HOSTETTER.

Received August 2, 1919.

Iron occurs in determinable amounts in a surprisingly large number of materials. In the course of work on the raw materials for optical glass the determination of this element soon became the most pertinent criterion of quality, inasmuch as iron introduced into the glass produces color, with a corresponding absorption of light, and lowering of the usefulness of the glass.

In the preparation of solutions of these raw materials for the determination of iron it was observed that the color of the hydrochloric acid solution was a convenient index to the amount of iron actually present. The iron in these solutions was subsequently titrated electrometrically and experience soon indicated that a method for iron based on this color could be made to yield results sufficiently accurate for average control work. The subject was later studied somewhat more in detail and the present note gives the results of experiments undertaken to establish conditions for the development of this color, the effects of acids and salts, the precision attainable, and also certain applications of the method as finally developed. Several interesting lines of research were suggested by these experiments but, unfortunately, time was not available for other investigation than that necessary for the development of an analytical procedure.

The yellow color developed by ferric chloride in hydrochloric acid solution has been used as an indicator in the direct determination of iron by titration with stannous chloride,[1] the disappearance of the color indicating complete reduction of the iron. Similarly, the appearance of the yellow color is used as an indicator in the determination of tin by titration with ferric chloride.[2] Advantage has also been taken of the color of ferric chloride solutions in the development of color standards for use in drug assays.[3] The application of this color to the determination of iron was proposed by Hüttner in 1914,[4] but has received very little, if any, recognition; his results will be presented later. Reference will also be made in the course of the text to the older investigations of Müller on the change of color of ferric chloride solutions under different conditions. The researches of Schaer on the color of solutions of iron salts should also be noted here.[5]

The color produced by ferric chloride in hydrochloric acid solution has been investigated by Donnan and Bassett, who attribute it to the formation of some negative ion since, under electrolysis, the color moves toward the anode.[6] Three colored crystalline hydrates of $Fe_2Cl_6.2HCl$ have been described by Roozeboom and Schreinemakers[7] and probably the color developed in solution arises from these, or similar, compounds.

Method of Study.

The colors developed by ferric iron in hydrochloric acid under definite conditions were compared with the color produced by a certain quantity of iron under known conditions, taken as the standard. After a series of comparisons had been made the results, of course, could be transferred by calculation to any other basis and this was done in certain experiments. The standard ferric solution first used was made up from ferric alum, the actual iron content being determined by electrometric titration with 0.01 *N* potassium dichromate solution and also by precipitation with ammonia. Later, standard solutions were made up determinate by dissolving ferric oxide in 1 : 1 hydrochloric acid.

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[1] W. W. Scott, *Standard Methods of Chemical Analysis*, 1917, p. 221.

[2] C. Mene, *Compt. rend.*, 31, 82 (1850).

[3] H. V. Arny and C. H. Ring, *J. Ind. Eng. Chem.*, 8, 309–317 (1916).

[4] *Z. anorg. Chem.*, 86, 341–357 (1914).

[5] *Arch. Pharm.*, 239, 257–283, 340–353 (1901).

[6] *J. Chem. Soc.*, 81, 955 (1902).

[7] *Z. physik. Chem.*, 15, 591 (1894).

In the earlier work the color comparisons were carried out in test tubes or small cylinders, no optical devices being used to facilitate the comparison or to make it more sensitive. Later a color comparator developed by H. E. Merwin of this Laboratory, and soon to be described by him, was used to good advantage and all of the comparisons were repeated with the new device. The heights of the solutions compared varied from 10 to 100 mm. and settings could be made to 0.5 mm. in the lower range and to 2 or 3 mm. at the greatest height.

Sensitivity of Method.

The amounts of iron which were present in our materials ranged from 0.001% to 0.1% Fe_2O_3. The iron content for the most part fell within the range of 0.005 to 0.02% and an accuracy of 25% on the lower, and of 10 to 15% on the higher amount was satisfactory. On a 10 g. sample, 0.01% corresponds to 1 mg. of ferric oxide; this amount of oxide in 25 cc. of acid can be readily determined colorimetrically within 10%.

Hüttner[1] states that a solution containing 1 part iron in 100,000 possesses a significant yellow color.[2]

It has been found in this study of the color that a solution of 0.02 mg. of ferric iron in 50 cc. of 1 : 1 hydrochloric acid shows a detectable color when viewed lengthwise against a white background through a layer 18 mm. in height. The color developed by $^1/_2$ this quantity of iron under the same conditions is barely perceptible even when compared with pure acid (1 : 1). This sensitivity is ample for most work, but when necessary it may be increased by using more concentrated acid, or by adding calcium chloride.[3]

A good idea as to the intensity of this coloration may be had from the fact that the color intensity of a peroxidized titanium solution (developed

[1] *Loc. cit.*, p. 346.

[2] Morgan, in a study of Mene's method for tin, has shown that the amount of ferric chloride necessary to produce a coloration at the end-point may be lessened by viewing a Bunsen flame through the solution; under these conditions the flame takes on a greenish color as soon as a trace of ferric iron in excess is added, and 0.035 mg. of ferric iron in 25 cc. may be detected in this manner. (*J. Anal. App. Chem.*, **2**, 169 (1888). Taken from Mellor, *A Treatise on Quantitative Inorganic Analysis*, **1913**, p. 310.)

[3] Cf. *postea*.

under standard conditions[1]) is, approximately, 16 times the intensity of color developed by an equal weight of iron in 1 : 1 hydrochloric acid when the height of the iron solution (containing 0.5 mg. of ferric oxide per cc.) is about 100 mm. This test was very kindly made by my colleague, Dr. H. E. Merwin. Exact comparison, however, could not be made since the hue of the iron solution was slightly yellower than that of the titanium solution. Both solutions were orange-yellow.

Permanency of Color.

Arny and Ring[1] state that the original acidulated solution of ferric chloride neither fades nor precipitates to a perceptible degree within two years. Experiments carried out in the course of this study showed definitely that no change of color took place within 2 or 3 weeks, and although longer time tests were not made it is probable that the colors of acidified ferric chloride solutions are fully as stable as stated by the above mentioned authors.

Relative Color Intensity.

The term "relative color intensity" used here is defined as the ratio of the depth of the standard solution to the depth of the test solution when matched. Expressed otherwise, it is the color intensity developed by a quantity of iron under certain conditions, as compared to the color intensity developed by the same amount of iron under the standard conditions. The solution used as a standard is defined by the concentrations of iron and of acid at a given temperature; these conditions are expressed on the graphs in Figs. 1 to 4.

Effect of Temperature upon Color Intensity.

The effect of temperature upon the color developed by ferric iron in hydrochloric acid was studied by comparing the color developed in a standard acid solution held at 30° with the color of another portion of the same solution heated, or cooled, to some other temperature. The color intensity increases with elevation of temperature and it was also found *that the relative increase depends upon the concentration of iron* in the solution—the more concentrated the iron solution the greater the increase produced by a given temperature rise until a concentration of 0.5 mg. of iron per cc. is reached, after which doubling the concentration causes very little, if any, change in the temperature coefficient. The measurements made in this series of tests are subject to two errors which could have been avoided only by the development of special apparatus. The first error was that caused by the temperature changing during a comparison, and the second was the formation of a mist in the tube above the hot solution developed by the condensation of hydrochloric acid and moisture. The curves shown in Fig. 1 are the most representative that could be passed through points deviating by as much as 15% (maximum). The standard color for each series was the color produced by the same amount of iron in hydrochloric acid (18.8% HCl) held at 30°.

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[1] H. E. Merwin, *Am. J. Sci.*, 28, 119–125 (1909).

[2] *Loc. cit.*

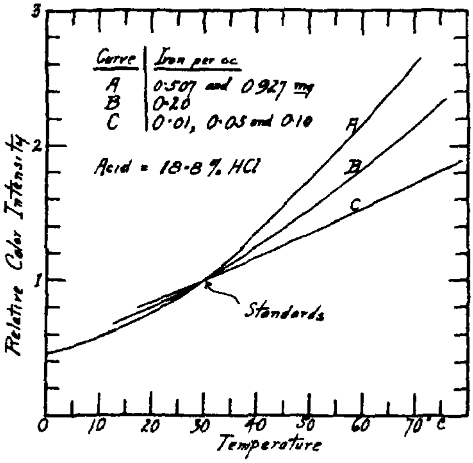

Fig. 1.—Showing the change of color intensity with temperature for hydrochloric acid solutions of ferric chloride containing different concentrations of iron. The color developed at 30° is taken as the standard for each solution studied. The temperature coefficient increases with the iron concentration. All solutions were made up in 18 8% HCl

From the slopes of the curves near 30° the temperature coefficient is found to be approximately 1.7% per degree for dilute solutions containing up to 0.1 mg. of iron per cc.; that for solutions containing 0.2 mg. of iron per cc. the coefficient is 2.3% per degree, while for solutions containing 0.5 mg. or more per cc. the coefficient rises to 2.9% per degree. The coefficients just given are approximate values obtained under the conditions described and apply only to these conditions. It is quite probable that the coefficient changes with acid concentration and the curves of Fig. 2 shortly to be described support this view. It is also probable that there is a time lag in the change of color on heating or cooling.

We may note here that Müller[1] found that an elevation of 30° increased the color intensity of a ferric chloride solution from 1 to 1.4 or 1.5, a result which agrees well with those plotted in Curve B.

Dependence of Color Intensity upon Acid Concentration.

Effect of Hydrochloric Acid.—It is a matter of common observation that the intensity of the color developed by a certain amount of ferric iron in hydrochloric acid depends upon the concentration of the acid. Müller[1] pointed out in 1874 that the color intensity of a feebly acidified solution of ferric chloride decreases by dilution with water more rapidly than in a strictly inverse proportion to the increase of volume. He also showed that hydrochloric acid increases the "specific intensity" of ferric chloride solutions. Hüttner made a study of the effect of acid concentration on the color intensity and found that the intensity passed through a maximum at about 28% HCl. He carried out this test at 18°, using a solution containing 1 part of iron to 20,000. His results, recalculated to another acidity basis, are shown in the dotted curve on Fig. 2, which also gives some values obtained in my repetition of his work. The agreement is quite satisfactory.[2] It is interesting to call attention here to the lower intensification obtained at a higher temperature as shown by the curve for 27°.

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[1] A. Müller, *Pogg. Ann. Ergänzungs-b.*, 6, 123–141 (1874).

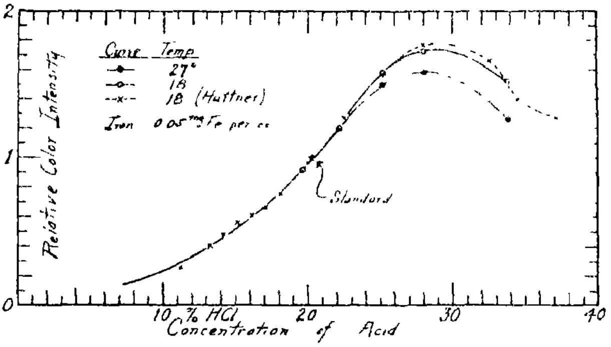

Fig. 2.—Showing the change of color intensity as the concentration of hydrochloric acid increases. The broken line gives the results obtained by Huttner recalculated to a different standard. Note the change of relative intensification produced by a change of temperature. The color produced in acid of constant-boiling composition is taken as the standard.

In this detailed study of the effect of hydrochloric acid on the color intensity, iron solutions containing various concentrations of acid were matched against an iron solution made up in constant-boiling hydrochloric acid (20.24% HCl)[3] containing the same amount of iron. The results obtained in this test are shown in Fig. 3; they may be summarized as follows: (1) The relative color intensity increases from about 0.20 at 9% acid to 1.4–2.4 at higher acidities (26 to 30% HCl) and then decreases as the acid reaches its maximum concentration. (2) Below 20.24% HCl (taken as the standard), the relative intensity change is independent of the iron concentration, but above this concentration the change produced depends upon the amount of iron present. A solution containing 0.5 mg. of iron per cc. reaches a maximum color intensity of 2.4, a solution containing 0.2 mg. iron per cc. goes through a maximum of 1.9, while a dilute solution containing 0.007 mg. per cc. rises only to 1.5 in comparison with the color developed by these amounts of iron in 20.24% HCl. (3) The acid concentration at which the maximum development of color intensity takes place likewise depends upon the concentration of iron. For the dilute solution containing only 0.007 mg. iron per cc. the maximum is reached at about 26% acid, with higher iron concentrations the maximum takes place at successively higher acid concentrations reaching over 30% when the iron present amounts to 0.5 mg. per cc.

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[1] *Loc. cit.*

[2] The acid available was, unfortunately, not sufficiently concentrated to permit the covering of the entire range studied by Huttner. The label on the bottle claimed a sp. gr. of 1.18 to 1.19 and an acid content of 35.5 to 37.5 HCl, but actually the sp. gr. (15/15) was found to be only 1.172 corresponding to about 33.8% HCl.

[3] Hulett and Bonner, THIS JOURNAL, **31**, 390–393 (1909).

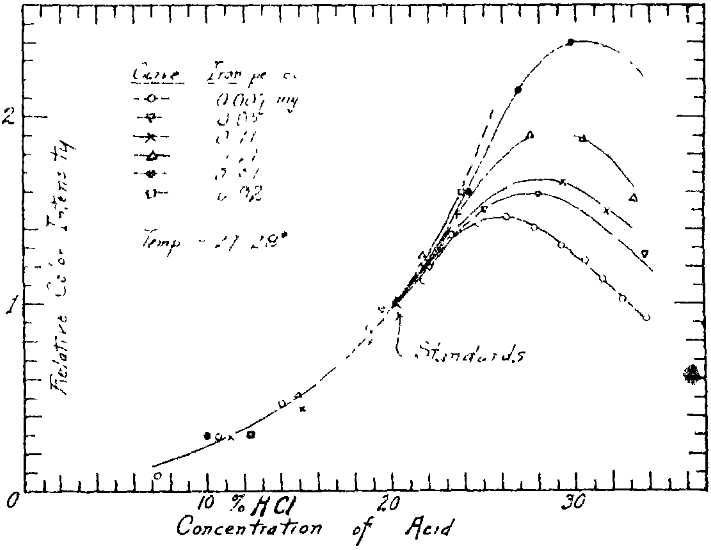

Fig. 3. Showing how the intensification caused by increase of acidity depends upon the concentration of iron. The standard color is that produced by the given concentration of iron in constant boiling hydrochloric acid.

The advantage of the increase of intensity gained by working at high acidities is only apparent because of the fact that the relative intensification is a function of the iron concentration. However, at 20% acid concentration this criticism no longer applies and this is the acid composition actually used in the final method. The disadvantage of working in a region where the color intensity is changing rapidly with acid concentration—as in the neighborhood of 20% acid—is more than counin further detail the effect of a high concentration of chloride on the color being studied. This was done by adding successively larger quantities of the salt to portions of a standard iron solution and comparing the resulting colors. The calcium chloride was hydrated to the extent of 25% and this additional water content was considered in calculating the acidity of the final solution. Some of the effects found in the earlier experiments indicated that the intensifying effect brought about by calcium chloride is a function of the acid concentration and this was confirmed by the final series, the results of which are shown in Fig. 4. The curves show the maxima which seem to be characteristic of the effect of acid on the color but the maximum occurs in more dilute acid as the concentration of calcium chloride is increased. It is quite probable that the increase of intensification caused by the chloride depends also on the iron concentration.

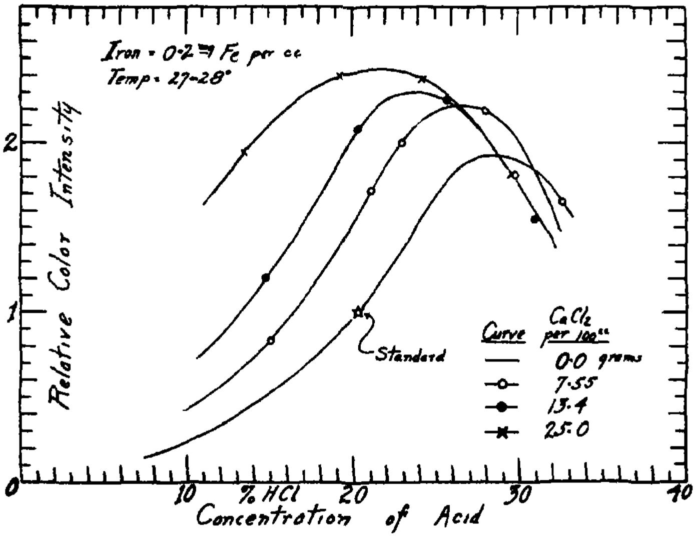

Fig. 4.—Showing the effect of calcium chloride on the change of color intensity caused by varying the concentration of acid. *All* the curves have been made by comparison with the color produced by 0.2 mg. of ferric iron per cc. of constant-boiling hydrochloric acid.

The results obtained on the action of salts on the color intensity of ferric chloride solutions indicate that correction should be made for the change of intensity caused by the salt, or, more accurately, the standard should be made up with equivalent quantities of the salt. The results given by Hüttner on the iron contents of certain metals, such as tin and zinc which form very soluble chlorides, may be too high because of the intensifying effect of the chlorides, which apparently was not recognized by Hüttner. The addition of calcium chloride, if iron-free material is available, furnishes a simple method of increasing the color intensity for a given amount of iron, which may be useful in certain cases.

Interfering Substances.

It is obvious that colored metallic chlorides must be absent from the solution to be compared for color. In such cases the iron must first be separated from such metals and the procedure to be used for this separation will depend upon the nature of the interfering substance. The iron must also be separated from nitrates before color comparison can be made since the interaction between strong hydrochloric acid and the nitrate would form colored products which would obviously interfere. In these cases the iron is conveniently precipitated from the solution by ammonia after the addition of alum solution. The aluminous precipitate carries the iron hydroxide with it; the precipitate is readily filtered off and is dissolved in 1 : 1 hydrochloric acid.

It has also been found that samples of salts will frequently contain organic matter, sometimes in the form of wood fibers, or chips, which will develop a deep yellow color when boiled with hydrochloric acid. To avoid this difficulty the iron should be precipitated with ammonia after all the iron-bearing scale has been dissolved in acid; the precipitate is dissolved off the filter in cold acid which, for the short time of contact, does not acquire color from the organic matter caught on the filter.

If the iron is not fully oxidized it must be changed to the ferric condition by treatment with an oxidizing agent. Unfortunately, this adds another complication since, if excess of oxidizer is added, other products, such as chlorine, are liberated which interfere with the colorimetric determination because of the additional color produced thereby.

In case it is necessary to oxidize the iron it may be done with nitric acid, hydrogen peroxide, etc., after which the iron must be precipitated with ammonia, alum solution having previously been added. Hüttner treats the solution with potassium chlorate, boiling off the excess of free chlorine.

Solution of Iron Scale.

Iron may exist as an impurity in salts and oxides in several forms, and failure to recognize the nature of the iron-bearing material may lead to large errors in the determination of this element. Precautions similar to those found to be necessary in an exact determination of iron in sand[1] for instance, are not confined to mineral products and may be used to illustrate the importance of knowing the nature of the iron-bearing materials, if these are to be decomposed and the iron content determined. In most salts and oxides iron was found to be present to a greater or less extent as "scale" derived from iron apparatus used in the manufacturing processes. This scale is essentially an oxide of iron and is very resistant to the action of sulfuric and nitric acids which dissolve it very slowly. Hydrochloric acid, on the other hand, will dissolve this scale if the action takes place at an elevated temperature and is sufficiently prolonged. The presence of this scale can be readily demonstrated in many salts by dissolving from 10 to 100 g. of the salt in water or in dil. acid and examining the slight residue which usually remains. This is a severe test and many highly purified chemical reagents will show in a concentrated solution of this kind foreign material suspended throughout the solution or on the bottom of the beaker. The iron scale is usually magnetic and test with a hand magnet will demonstrate its presence.

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[1] J. B. Ferguson, *J. Ind. Eng. Chem.*, 9, 941–943 (1917).

The fact that iron scale of this sort is not readily dissolved by nitric or sulfuric acids indicates at once that analytical methods which decompose the sample with these acids will give low results for iron if no further precautions are taken. This has actually been found to be the case in certain materials—our results, obtained in hydrochloric acid solution, being higher, frequently by many times, than those found by the manufacturer of the chemical.

Iron occurring as the salt of the acid present in the chemical may in general be brought into solution by acids other than hydrochloric but our experience indicates that one must always assume the presence of iron scale and consequently take precautions to insure its decomposition.

Results Obtained with this Colorimetric Method.

A few results may be quoted here to show the agreement obtained with the hydrochloric acid color method for total iron and the electrometric method[1] on the same material. It is a pleasure to acknowledge here the assistance of Mr. E. C. Baum, of the Armour Fertilizer Works, in making these analyses.

TABLE II.

Total Iron as Fe_2O_3.

Material	Electrometric	Colorimetric
Potassium carbonate...........	0.046% 0.041 0.042	0.040%
Potassium carbonate...........	0.032	0.030
Potassium carbonate...........	0.022	0.020
Potassium carbonate...........	0 0276	0.028
Potassium carbonate...........	0.0090	0.010
Precipitated silica.............	0.251	0.250

Summary.

Conditions have been found under which the yellow color developed by dissolving ferric iron in hydrochloric acid may be used for the determination of iron. The temperature coefficient for this color varies from 2 to 3% per degree depending on the concentration of iron and probably also on the acidity. The color developed by a given amount of iron varies with the acid concentration, reaching the maximum intensity at from 26 to 28% HCl. The relative increase produced by acid is greater the higher the concentration of iron; this is especially true above 20% HCl, but below this concentration the relative change is independent of the iron content. Inasmuch as solutions must frequently be boiled in order to insure the complete solution of iron present as "scale" the use of constant-boiling acid is recommended and its use has been found to be altogether satisfactory. The effects of salts on the color indicate that sulfates cause bleaching, and chlorides intensification; detailed study of the effect of the very soluble calcium chloride shows that an intensification of 2.5 may be attained by the addition of this salt, consequently when testing for iron in a very soluble chloride the standard iron solution must be made up to possess the same salt concentration.

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[1] J. C. Hostetter and H. S. Roberts, THIS JOURNAL, 41, 1337–1357 (1919).

Some applications of the method are given and certain results presented.

WASHINGTON, D. C.

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF THE GENERAL ELECTRIC COMPANY.]

ISOMORPHISM, ISOSTERISM AND COVALENCE.

BY IRVING LANGMUIR.

Received June 30, 1919

In recent papers[1] I have described a theory of valence which I have called the octet theory. This theory is based upon and is essentially an extension of G. N. Lewis' theory of the "cubical atom."[2] According to this theory each bond between adjacent atoms in organic compounds corresponds to a pair of electrons held in common by the two atoms. Since in other types of compounds the number of pairs of electrons held in common is not always the same as the number of valence bonds that have usually been assumed I proposed that the number of pairs of electrons which any given atom shares with the adjacent atoms be called the covalence of that atom. It was then shown that the covalence of carbon is always 4, that of nitrogen is usually 3 or 4, while that of oxygen is 1, 2 or sometimes 3, etc.

The octet theory indicates that the number and arrangement of electrons in the nitrogen molecule, the carbon monoxide molecule, and the cyanogen ion, is the same, and it was shown in fact that the physical properties of nitrogen and carbon monoxide are remarkably alike.

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[1] A simpler exposition of the theory and its applications is given by Elwood Hendrick, *Met. Chem. Eng.*, 21, 73 (1919), July 15th; Langmuir, *J. Frank. Inst.*, 187, 359 (1919); THIS JOURNAL, 41, 868–934 (1919); *Proc. Nat. Acad. Sci.*, 5, 252 (1919).

[2] G. N. Lewis, THIS JOURNAL, 38, 762 (1916).

A similar relationship was found to exist between nitrous oxide and carbon dioxide and again between cyanic and hydronitric acid.

The following data, taken from Landolt-Börnstein's tables and Abegg's handbook, show the extraordinary agreement between physical properties of carbon dioxide and nitrous oxide·

	N_2O	CO_2
Critical pressure, atm	75	77
Critical temp	35 4°	31 9°
Viscosity at 20°	148×10^{-6}	148×10^{-6}
Heat conductivity at 100°	0 0506	0 0506
Density of liquid at —20°	0 996	1 031
Density of liquid at +10°	0 856	0 858
Refractive index of liquid, D line, 16°	1 193	1 190
Dielectric constant of liquid at 0°	1 598	1 582
Magnetic susceptibility of gas at 40 atm , 16°	$0\ 12 \times 10^{-6}$	$0\ 12 \times 10^{-6}$
Solubility in water 0°	1 305	1 780
Solubility in alcohol at 15°	3 25	3 13

Both gases form hydrates, $N_2O.6H_2O$ and $CO_2.6H_2O$. The vapor pressure of the hydrate of nitrous oxide is 5 atm at —6°, whereas the hydrate of carbon dioxide has this vapor pressure at —9°. The heats of formation of the two hydrates are given, respectively, as 14900 and 15000 calories per mol. The surface tension of liquid nitrous oxide is 2.9 dynes per cm. at 12.2°, while carbon dioxide has this same surface tension at 9.0°. Thus nitrous oxide at any given temperature has properties practically identical with those of carbon dioxide at a temperature 3° lower.

There is one property, however, which is in marked contrast to those given above. The freezing point of nitrous oxide is —102°, while that of carbon dioxide is —56°. This fact may be taken as an indication that the freezing point is a property which is abnormally sensitive to even slight differences in structure. The evidences seem to indicate that the molecule of carbon dioxide is more symmetrical, and has a slightly weaker external field of force than that of nitrous oxide. Such differences could easily be produced by the difference in the charges on the kernels, and may also be taken as evidence that the structure of nitrous oxide is represented by $N = N = O$ rather than $N = O = N$.

Compounds showing a relationship to one another like that between carbon dioxide and nitrous oxide will be called isosteric compounds, or isosteres. These terms, however, are not to be restricted to chemical compounds but are applicable to chemical radicals or to groups of atoms which hold pairs of electrons in common. A comolecule is defined as a group of atoms held together by pairs of electrons shared by adjacent atoms. Comolecules are thus isosteric if they contain the same number and arrangement of electrons. The comolecules of isosteres must, therefore, contain the same number of atoms. The essential differences between isosteres are confined to the charges on the nuclei of the constituent atoms. Thus in carbon dioxide the charges on the nuclei of the carbon and oxygen atoms are 6 and 8, respectively, and there are $2 \times 8 + 6 = 22$ electrons in the molecule. In nitrous oxide the number of charges on the nitrogen nuclei is 7, but the total number of electrons in the molecule is again $2 \times 7 + 8 = 22$ The remarkable similarity of the physical properties of these two substances proves that their electrons are arranged in the same manner.

According to the object theory we may expect the following types of isosteres

TABLE I

List of Isosteres

Type	
1	H^-, He, Li^+
2	O^{--}, F^-, Ne, Na^+, Mg^{++}, Al^{+++}
3	S^{--}, Cl^-, A, K^+, Ca^{++}
4	Cu^+, Zn^{++}
5	Br^- Kr, Rb^+, Sr^{++}
6	Ag^+, Cd^{++}
7	I^-, Xe, Cs^+, Ba^{++}
8	N_2, CO, CN^-
9	CH_4, NH_4^+
10	CO_2, N_2O, N_3^-, CNO^-
11	NO_3^-, CO_3^{--}
12	NO_2^-, O_3
13	HF, OH^-
14	ClO_4^-, SO_4^{--}, PO_4^{---}
15	ClO_3^-, SO_3^{--}, PO_3^{---}
16	SO_3, PO_3^-
17	$S_2O_6^{--}$, $P_2O_6^{----}$
18	$S_2O_7^{--}$, $P_2O_7^{----}$
19	SiH_4, PH_4^+
20	MnO_4^-, CrO_4^{--}
21	SeO_4^{--}, AsO_4^{---}

All the comolecules given under any one type are isosteric with one another.

When isosteric comolecules are also isoelectric, that is when they have the same total charge on the comolecules, all their physical properties should be closely similar. In Table I the only pairs of comolecules which are also isoelectric are (8) N_2 and CO, (10*a*) CO_2 and N_2O, and (10*b*) N_3^- and NCO^-.

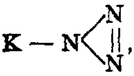
I have already pointed out that the physical properties of the first two pairs of substances (8 and 10*a*) furnish proof of the similarity of structure predicted by the octet theory, and show the usefulness of the conception of isosterism.

The isosterism of the cyanate and trinitride ions applies of course also to compounds derived from them. Thus we should expect HNCO and HN_3 to be isosteric as well as pairs of compounds such as $KNCO-KN_3$, $Ba(NCO)_2-Ba(N_3)_2$, etc.

There are, unfortunately, very few data on the physical properties of cyanates and trinitrides. Both cyanic and hydronitric acids are liquids at 0° and both explode on heating. Apparently the freezing point of cyanic acid has not been determined. In a general way the solubilities of the salts of these two acids are known to be similar; the potassium and the barium salts of both acids are readily soluble in water, while the lead and silver salts are very difficultly soluble.

Groth[1] gives the following crystallographic data for anhydrous potassium cyanate and trinitride. Both belong to the tetragonal system. The ratio of the axes $a : c$ is $1 : 0.5766$ for the cyanate and $1 : 0.5798$ for the trinitride. Both have "strong negative double refraction." The most common faces of both crystals are given as C (001) and O (111). Cleavage was not observed in either case. No other data are given by Groth from which a comparison of cyanates and trinitrides can be made.

From the octet theory and the above data it is therefore safe to predict that the physical properties of the salts of cyanic and hydronitric acids will be found to be practically identical. This resemblance should be at least as close as that between nitrous oxide and carbon dioxide and should cover solubility in water, in alcohol, etc., density in crystalline form and in solutions, viscosity of solutions, optical and magnetic properties, electric conductivity of solutions, etc. The densities should be alike because the molecular weight of N_3 is the same as that of NCO.

The available experimental data, although meager, are sufficient, I think, to show the complete isomorphism of cyanates and trinitrides. The similarity of structure thus follows directly from Mitscherlich's rule. These experimental data furnish direct evidence against such structural formulas as  $\mathrm{K-N}\left\langle\begin{matrix}\mathrm{N}\\ \| \\ \mathrm{N}\end{matrix}\right.$, $\mathrm{K-N=N\equiv N}$, $\mathrm{K-O-C\equiv N}$, but strongly support the octet theory structures:

$$K^+(N = C = O)^- \quad \text{and} \quad K^+(N = N = N)^-$$

These formulas show that the covalence of potassium is zero; the nitrogen and oxygen in the cyanate are dicovalent, while in the trinitride one of the nitrogens is quadricovalent and the other two are dicovalent. These data, as far as they go, thus constitute experimental proof of the octet theory of valence. Further experimental work on the physical properties of cyanates and trinitrides is highly desirable.

The octet theory also indicates that diazomethane should have the structure $H_2C = N = N$ and should thus be isosteric with $H_2C = C = O$, a compound apparently not given in Beilstein. This compound should closely resemble diazomethane in all its physical properties such as freezing point, vapor pressure, viscosity, etc.

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[1] P. Groth, "Chemische Krystallographie," Leipzig, Part I, 1906, Part II, 1908.

No direct comparison can be made of the physical properties of isosteres having different electric charges. Thus we should not expect sodium salts to resemble neon, even though the sodium ion is an isostere of the neon atom—the electric force around the ion is sufficient to account for the differences in physical properties.

There is, however, another way in which the actual isosterism of comolecules with different charges can be tested from experimental data. It is evident that if any two substances are very much alike in physical properties, then any isoelectric isosteres of these substances should show similarly close relationships with one another. For example, in Types 3 and 8 of Table I, we find argon and nitrogen resemble each other closely. Therefore the chlorine ion, isosteric with argon, should have a close resemblance to the cyanogen ion which is isosteric with nitrogen. The striking similarity of chlorides and cyanides is thus directly correlated with that between argon and nitrogen.

In an exactly similar manner the close relationship between potassium salts and ammonium salts can be derived from the similarity between the physical properties of argon and methane. For from Table I (Types 3 and 9) the potassium ion is isosteric with argon, while the ammonium ion is an isostere of methane. Of course the potassium ion and the ammonium ion are not isosteres of one another. The resemblance between potassium and ammonium salts is of a much lower order than that between truly isosteric substances such as nitrous oxide and carbon dioxide, or between salts of cyanic and hydronitric acids. The octet theory indicates in fact that the potassium ion is cubic in form, while the ammonium ion, like methane, must have a tetrahedral symmetry. This conclusion is in accord with the crystal structures of potassium chloride and ammonium chloride. Bragg[1] has found that in potassium chloride each potassium ion is surrounded by 6 equidistant chlorine ions, arranged just as if the crystal were built up of cubical potassium and chlorine ions with their faces in contact; but finds that ammonium chloride, although it crystallizes in the isometric system, is in no sense isomorphous with the other alkaline halides. Each ammonium ion is surrounded by 8 equidistant chlorine ions arranged like the corners of a cube about its center. This indicates that the tetrahedral ammonium ions force the chlorine ions to arrange themselves symmetrically with respect to the 4 faces or corners of the tetrahedron, while the cubical potassium ions permit the simpler cubic packing. Ammonium and potassium sulfates, however, are isomorphous, for the larger volume of the sulfate ion causes its influence to predominate over the slight differences between the forces around the two positive ions.

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[1] W. H. Bragg and W. L. Bragg, "X-Rays and Crystal Structure," London, 1916, pp. 95 and 158.

The nitrates and perchlorates of all metals are readily soluble and most of them are deliquescent. From this similarity of properties we may conclude that the other isosteres of Types 11 and 14 of Table I should be interrelated. Thus carbonates and sulfates should show a general resemblance to each other in their solubilities.

The smaller solubility of salts of divalent ions is, of course, due to the greater forces holding the divalent ions, making it more difficult for them to separate. The process of solution of salts involves, according to the octet theory, the separation of the ions. Thus sulfates and carbonates of most metals are difficultly soluble compared to the nitrates and perchlorates. Salts like lead and barium carbonates and sulfates in which both ions are divalent, are thus particularly difficultly soluble.

Boron nitride, which consists of tervalent ions, has still greater stability, and is infusible and insoluble in all solvents.

The observed differences between the ordinary properties of the differently charged isosteres are thus to be expected. But there is one property, namely crystalline form, which should depend on the arrangement of the electrons in substances rather than upon the magnitude of the forces between their atoms. By a comparison of crystal forms it should therefore be possible to obtain direct evidence of the similarity of the arrangement of the electrons in isosteric substances even if the charges on the comolecules are different.

For example, since the sodium ion and the fluorine ion are isosteric and cubic in form, we should expect them to pack together in a crystal lattice in exactly the way that Bragg has found they do. The magnesium and oxygen ions, however, are also isosteric with the sodium and fluorine ions, so that we should expect magnesium oxide to have a crystal structure identical in form with that of sodium fluoride. According to Groth both substances are cubic, sometimes crystallizing as octahedra, and both show good cleavage parallel to the (100) plane. To answer the question thus raised, Dr. A. W. Hull has studied the X-ray patterns obtained with magnesium oxide and sodium fluoride and has thus recently found[1] that the crystal structures of both substances are alike, except that the atoms in magnesium oxide are drawn closer together by the greater forces. Thus magnesium oxide and sodium fluoride should be looked upon as isomorphous. By the octet theory the covalences of all the atoms in these substances are zero, since they do not share electrons with each other. The isomorphism is thus in full accord with Mitscherlich's rule by which isomorphous substances should have similar structures. Since the ions O^{--}, F^-, Na^+ and Mg^{++} are isosteric we should also expect that MgF_2 and Na_2O should be isomorphous. Groth states that sodium oxide has not been obtained in the form of well developed crystals. However, by Hull's method of X-ray analysis, substances can now be studied in powdered form so that we may hope to see whether in fact these two substances are isomorphous. Other pairs of substances which may be isomorphous are potassium chloride and calcium sulfide, potassium sulfide and calcium chloride, cuprous sulfide and zinc chloride, etc.

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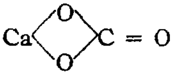
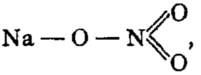
[1] Soon to be published.

A still more interesting class of isomorphous substances which are predicted by the octet theory is that represented by sodium nitrate and calcium carbonate. Since the nitrate and carbonate ions are isosteric we should expect sodium nitrate and magnesium carbonate to be isomorphous, Na^+ and Mg^{++} being isosteric. As a matter of fact, both substances are given by Groth as trigonal scalenohedral with the ratio of the axes 1 : 0.8297 and 1 : 0.8095, respectively.

The practical identity in all the crystallographic properties of sodium nitrate and calcium carbonate has long been known. In Mitscherlich's early theory before clear ideas of valence were developed, no difficulty was experienced in regarding these two substances as isomorphous and as having similar structures. The theory of valence, however, gave formulas  and , so that they could no longer be regarded as of similar structure. It was necessary either to abandon Mitscherlich's rule or to re-define isomorphism so as to exclude cases of this kind. Therefore Kopp[1] and Retgers[2] regarded substances as isomorphous only when they are capable of forming *mixed crystals*. This effectually eliminated such cases as sodium nitrate and calcium carbonate because mixed crystals can naturally only be obtained when the solubilities of the two substances are not too widely different. The crystal form depends, of course, exclusively, on the arrangement of the atoms and the electrons in them, while the ability to form mixed crystals depends on both similarity of arrangement and on similarity in the magnitude of the forces acting between the atoms. Thus Kopp found a practical rule by which nearly all those cases inconsistent with the ordinary valence theory, could be excluded. In order to be isomorphous in Kopp's sense, two substances must have atoms which are not only linked together in the same manner, but also have the same number of available electrons in corresponding atoms.

T. V. Barker,[3] however, and a few others crystallographers have maintained that isomorphism should be used to denote similarity of crystal form. Barker pointed out a great many new cases of isomorphism between substances which according to the ordinary valence theory are not closely related. Among these he mentions as types KIO_4–$CaWO_4$, $KClO_4$–$BaSO_4$–KBF_4, K_2SO_4–K_2BeF_4, and $NaNO_3$–$CaCO_3$ He shows how these cases of isomorphism are inconsistent with the ordinary valence theory, but are in a general way in agreement with Werner's coordination theory.

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[1] *Ber.*, 12, 868 (1879).

[2] *Z. physik. Chem.*, 3, 497 (1889), and later papers in 1889 to 1896.

[3] *Trans. Chem. Soc.*, 101, 2484 (1912).

By examining Table I it is evident that we should expect the following cases of isomorphism of the kind just considered

TABLE II

Typical Cases of Isomorphism Based on Isosterism

Type Table I	
2	(*a*) NaF–MgO (*b*) MgF_2–Na_2O
3	(*a*) KCl–CaS, (*b*) $CaCl_2$–K_2S
5	(*a*) $RbBr$–$SrSe$, (*c*) $SrBr_2$–Rb_2Se
7	(*a*) CsI–$BaTe$, (*c*) BaI_2–Cs_2Te
8	N_2–CO
10	$KNCO$–KN_3, etc
11	(*a*) $NaNO_3$–$CaCO_3$, (*b*) KNO_3–$SrCO_3$
14	(*a*) $KClO_4$–$SrSO_4$, (*b*) $NaHSO_4$–$CaHPO_4$ (*c*) $KHSO_4$–$SrHPO_4$
15	(*a*) $NaClO_3$–$CaSO_3$, (*b*) $KHSO_3$–$SrHPO_3$
17	$Na_2S_2O_6$–$Ca_2P_2O_6$
18	$Na_2S_2O_7$–$Ca_2P_2O_7$
20	$RbMnO_4$–$BaCrO_4$
21	$MnSeO_4\ 2H_2O$–$FeAsO_4\ 2H_2O$

Sodium nitrate crystals resemble those of calcium carbonate a little more closely than those of magnesium carbonate, although the sodium ion is isosteric with the magnesium ion but not with the calcium ion The molecular volume of sodium nitrate is nearer to that of calcium carbonate than that of the magnesium compound The much larger forces in the compounds containing the divalent ions must tend to draw the atoms closer together. The substitution of the larger calcium ion in place of the magnesium ion offsets this difference, and this probably accounts for the closer resemblance between the sodium and the calcium compounds. This same relationship is noticed in other pairs of compounds. Since in these replacements calcium corresponds most nearly to sodium we should expect strontium to correspond to potassium and barium to rubidium. This is well borne out in every case The following tables illustrate the cases of isomorphism corresponding to Types 11 to 21, shown in Table II, for which data are given by Groth The pairs of substances at the head of each table are those given in Table II. The other substances are generally recognized as being isomorphous with one or the other member of these pairs.

TABLE III.

Nitrates and Carbonates Type 11 (*a*). Trigonal Scalenohedral.

	a	*c*	
$NaNO_3$	1	0.8297	
$CaCO_3$	1	0.8543	
$MgCO_3$	1	0.8095	
$MnCO_3$	1	0.8259	
KNO_3	1	0.8259	Stable above 128°

At high temperatures $RbNO_3$, $SrCO_3$ and $BaCO_3$ also give trigonal crystals

All these substances show strong negative double refraction and similar cleavage

TABLE IV

Nitrates and Carbonates, Type 11 (*b*) Orthorhombic Bipyramidal

	a	*b*	*c*
KNO_3	0.5910	1	0.7011
$SrCO_3$	0.6090	1	0.7237
$CaCO_3$	0.6228	1	0.7204
$BaCO_3$	0.5949	1	0.7413

Negative double refraction

TABLE V

Perchlorates and Sulfates Type 14 (*a*) Permanganates and Chromates, Type 20.
Orthorhombic Bipyramidal

	a	*b*	*c*	Cleavage	
$KClO_4$	0.7817	1	1.2793	*c*(001)	*m*(110)[1]
$SrSO_4$	0.7790	1	1.2800	*c*(001)	*m*(110)[1]
$RbMnO_4$	0.8311	1	1.3323		
$BaCrO_4$	0.8231	1	1.3232		
$RbClO_4$	0.7966	1	1.2879	*c*(001)	*m*(110)
$BaSO_4$	0.8152	1	1.3136	*c*(001)	*m*(110)[1]
$KMnO_4$	0.7972	1	1.2982	*c*(001)	*m*(110)[1]
$SrCrO_4$	0.9496	1	1.0352		
$CsClO_4$	0.8173	1	1.2976		
$CsMnO_4$	0.8683	1	1.3705		
$CaSO_4$	0.8932	1	1.0008		. .
NH_4ClO_4	0.7932	1	1.2808		

TABLE VI

Sulfates and Phosphates, Type 14 (*b*) Triclinic Pinacoid.

	a.	*b*	*c*	α	β	γ.
$NaHSO_4$[2]	0.6460	1	0.8346	85° 06′	88° 57′	86° 47′
$CaHPO_4$	0.6467	1	0.8244	84° 57′	89° 43′	85° 38′
$SrHAsO_4$ . .	0.6466	1	0.8346	86° 32′	89° 14′	87° 56′

[1] Incomplete cleavage

[2] Axes *b* and *c* have been interchanged in order to correspond to those used to form the other compounds. Where the angles α, β, γ, were greater than 90° their supplementary angles were chosen.

TABLE VII.

Sulfates and Phosphates, Type 14 (*c*). Orthorhombic Bipyramidal

	a	*b*	*c*
$SrHPO_4$[1]	0.8581	1	1.9431
$KHSO_4$	0.8609	1	1.9344

Both substances form 8- or 4-sided plates parallel to *c*(001) with (111) as the next most important face. The plane of the optic axis is (001).

TABLE VIII.

Selenates and Arsenates, Type 21. Orthorhombic Bipyramidal.

	a	*b*.	*c*
$MnSeO_4.2H_2O$	0.8849	1	0.9959
$FeAsO_4.2H_2O$	0.8658	1	0.9541

Plane of the optic axis (100) in both.

Groth gives no data for the Types 15(*a*), 15(*b*), 17 and 18 of Table II.

The results given in these tables afford the strongest kind of evidence for the octet theory of valence and prove that crystal form depends on the covalence of the atoms forming the substance rather than upon the valences given by the ordinary theory.

In every one of the cases where isomorphism is predicted by the octet theory (see Table II), we find that the data available in Groth's "Chemische Kristallographie" indicate an almost complete identity of crystalline form. The agreement between the pairs of substances given in Table II is in fact usually rather better than among most of the classical examples of isomorphism. For example, the agreement of the ratios of the axes for potassium perchlorate and strontium sulfate (Table V) is much closer than among the various chlorates or among the sulfates. Sodium nitrate crystals (Table III) are more nearly like calcium carbonate than these are like magnesium carbonate. Potassium nitrate (Table IV) shows better agreement with strontium carbonate than calcium carbonate (aragonite) does with barium carbonate. Sodium hydrogen sulfate (Table VI) agrees slightly better (in axial angles) with calcium hydrogen phosphate than this does with strontium hydrogen arsenate.

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[1] The measurements on $SrHPO_4$ and on $CaHPO_4$ given in Table VI were made by Schulten, *Bull Soc. franç mineral* **27**, 120 (1904).

According to Groth the ratio of the axes for $SrHPO_4$ was found to be 0.6477 : 1 : 0.8581 and the only faces measured were (100), (133), (203), (130), (230), (010). Groth states that the chosen orientation of the $CaHPO_4$ crystals was adopted because of the relationships to those of $SrHPO_4$.

For the substance $BaHPO_4$ which Schulten finds to be orthorhombic he gives the ratios 0.7133 : 1 : 0.8117, and considers that these ratios are related to those given above for $SrHPO_4$ (see Groth, p. 815) although the crystals are of "entirely different form." These facts make it clear that Schulten chose for this orthorhombic crystal the axial ratio *a* : *b* :: 0.6477 : 1 simply to make this ratio agree with *a* : *b* :: 0.6467 : 1 which he had obtained for the *triclinic* crystals of $CaHPO_4$ and which he supposed isomorphous with $SrHPO_4$ notwithstanding that they belonged to a different crystal system. If we multiply the *a* intercept 0.6477 by 3 and then interchange the *a* and *c* axes we obtain the ratios given above in Table VII The crystal faces which Schulten measured should thus be denoted by (100), (111), (201), (110), (210), and (010) instead of the absurd set of faces (100), (133), (203), (130), (230) and (010) given by Schulten. There is thus ample internal evidence for making this change in Schulten's data. We may conclude that there is no similarity in the ratios between the axes of the triclinic $CaHPO_4$, the orthorhombic $SrHPO_4$ and the orthorhombic $BaHPO_4$, but they represent 3 distinctly different crystal types.

In several of the cases in Table II we find that no data are given by Groth by which a comparison between the crystalline form of similarly constituted compounds can be made. For example (Type 15*a*), no anhydrous sulfites of divalent metals and no hydrated chlorates of univalent metals are given. Although sodium hydrogen sulfite is given, no phosphites of divalent metals have been measured.

It seems safe to predict that nearly all the remaining pairs of substances given in Table II will be found to be isomorphous when data become available. By Hull's method of X-ray analysis these comparisons are now possible even with powdered materials, so that most of the difficulties disappear that have heretofore prevented the accumulation of such data.

We have thus far considered cases in which the octet theory leads us to expect isomorphism not predicted by the ordinary theory of valence. Let us now consider those cases where the ordinary theory indicates isomorphism, but the octet theory does not. Examples of this kind are, (*a*) carbonates and sulfites, (*b*) chlorates and nitrates, (*c*) chlorates and metaphosphates.

According to the ordinary theory the sulfur in sulfites has a valence of 4 like that of carbon in carbonates. In chlorates and nitrates the central atom is supposed to have a valence of 5. By the octet theory, however, the covalence of sulfur in normal sulfites is 3, while that of carbon in carbonates is 4. In chlorates the covalence of chlorine is 3, while n metaphosphates that of the phosphorus is 4. A great deal of effort has been expended by chemists and crystallographers to prove cases of isomorphism between nitrates and chlorates. Groth says that carbonates and sulfites should be expected to be isomorphous and recommends that much more work be done in a comparative study of these salts—especially he advises attempting to prepare mixed crystals. In spite of this effort and the belief of chemists in the similarity of the constitutions of these compounds, there seem to be no convincing data indicating similarity of crystalline form in these cases. For example, Groth points out that potassium hydrogen carbonate and potassium hydrogen sulfite both belong to the monoclinic system, and that their crystals have the same habit. An examination of the data shows that both form crystals which are elongated in the direction of the *b*-axis. The following crystallographic data, however, prove that the substances are very far from isomorphous:

	a.	*b.*	*c*	*β.*
$KHCO_3$	2.6770	1	1.3115	103° 25′
$NaHCO_3$	0.7645	1	0.3582	93° 19′
$KHSO_3$	0.9276	1	2.2917	94° 46′

The ratios of the axes could hardly be more different, and there is a difference of 9° in the inclination of the axes. The sodium acid carbonate is also monoclinic but has quite different constants from either of the other compounds. No other anhydrous sulfites are given by Groth.

The following hydrated sulfites and carbonates given by Groth are the only ones that are comparable in constitution. Ammonium sulfite, $(NH_4)_2SO_3.H_2O$, is monoclinic while sodium carbonate, $Na_2CO_3.H_2O$, is orthorhombic. The compound $Na_2CO_3.7H_2O$ is orthorhombic but $Na_2SO_3.7H_2O$ is monoclinic. Finally, $MgCO_3.3H_2O$ crystallizes in the orthorhombic system, while $MgSO_3.3H_2O$ is "ditrigonal pyramidal." All of the available crystallographic data thus seem to indicate conclusively that sulfites and carbonates do not have similar constitutions.

The chlorates and nitrates usually have different crystalline forms, but in many cases it has been found possible to make mixed crystals containing as much as 10 or 15% of one or the other of the constituents. Sodium chlorate crystallizes in the cubic system isomorphous with sodium bromate, while sodium nitrate is trigonal. This form of sodium chlorate is normally produced either from aqueous solution or by cooling the molten mass. By slow evaporation of a strongly supersaturated aqueous solution it is possible to obtain sodium chlorate in a trigonal form with angles very much like those of sodium nitrate, and also having negative double refraction like that of sodium nitrate; this trigonal form of sodium chlorate is very unstable, and soon goes over into the cubic form even at room temperature. It was found possible to prepare mixed crystals of sodium nitrate and chorate containing as much as 22.5% of the chlorate. An unstable monoclinic form of sodium chlorate has also been prepared.

Potassium chlorate crystallizes only in the monoclinic form with axes inclined 109°, while potassium nitrate is orthorhombic. Notwithstanding the fact that the crystals belong to different systems, Groth states that potassium chlorate and sodium nitrate closely resemble each other. He does not believe that mixed crystals can be formed because the molecular volumes are so different. However, monoclinic mixed crystals of potassium chlorate and potassium nitrate up to 15% of the nitrate have been obtained, as well as orthorhombic mixed crystals, with 25% of the chlorate. This is considered to denote similarity of structure, notwithstanding the complete difference of crystal form between potassium nitrate and chlorate. Silver chlorate and bromate are tetragonal while silver nitrate is orthorhombic. The chlorate also forms cubic crystals isomorphous with sodium chlorate. Silver chlorate thus shows no resemblance to the nitrates.

Anhydrous calcium, strontium, and barium nitrates crystallize in the cubic system, but strontium chlorate $Sr(ClO_3)_2$ is orthorhombic with axial ratios, 0.9174 : 1 : 0.6003. It also exists in 3 other modifications, no one of which is cubic. However, even here it has been possible to make mixed crystals containing 7 to 12% of chlorate.

The salts $Mg(NO_3)_2.6H_2O$, $Ni(NO_3)_2.6H_2O$, $Co(NO_3)_2.6H_2O$, are monoclinic, the nickel and cobalt salts being isomorphous with each other but not with the magnesium salt. On the other hand, the corresponding chlorates of nickel and cobalt, $Ni(ClO_3)_2.6H_2O$, etc., and the bromates of magnesium, nickel, cobalt and zinc, $Mg(BrO_3)_2.6H_2O$, etc., are cubic. Only in one instance were mixed crystals obtained: $Zn(BrO_3)_2.6H_2O$ and $Co(NO_3)_2.6H_2O$ crystallizing together as cubic crystals.

Looking back over this comparison of chlorates and nitrates we see that among the 20 compounds considered (belonging to 5 different crystal systems), there is only one instance, namely that of sodium nitrate and the unstable trigonal modification of sodium chlorate, in which corresponding nitrates and chlorates even belong to the same system.

This evidence seems sufficient to prove that nitrates and chlorates have fundamentally different constitutions. A careful study of the trigonal form of sodium chlorate should be made, preferably by the X-ray method, to determine if its structure is actually like that of sodium nitrate. If it turns out to be so, it is probably to be explained as a very unusual form, in which two of the electrons in the atoms constituting the chlorate ion become unavailable, perhaps by being imprisoned within one of the octets. Under such conditions the chlorate ion might become "pseudo-isosteric" with the nitrate ion, so that the chlorine atom might then act with a covalency of 4.

There are no available data by which to test isomorphism between chlorates and metaphosphates.

These considerations show that the ordinary valence theory not only fails to predict cases of isomorphism which do exist (for example, potassium chlorate and strontium sulfate) but predicts isomorphism (sulfites and carbonates) where none exists. The octet theory does not fail in either of these ways. I have used the word isomorphism as expressing a close resemblance in crystallographic data. The data given in the cases of the nitrates and chlorates show conclusively in my mind that the formation of mixed crystals often occurs when there is no close resemblance in crystal structure. It seems therefore that this criterion should not be used to indicate similarity in chemical constitution. The question of course arises: how many other cases of mixed crystals could be found if the same effort were expended in looking for them among other types of compounds.

Let us now consider in more detail the cases of isomorphism given by Barker:

	a	b.	c.	β
A. Monoclinic.				
$CuTiF_6.4H_2O$	0.7471	1	0.5564	104° 9′
$CuCbOF_5.4H_2O$	0.7627	1	0.5629	103° 20′
$CuWO_2F_4.4H_2O$	0.7648	1	0.5629	103° 14′
B. Monoclinic.				
K_3HSnF_8	0.6277	1	0.4928	93°
K_3HCbOF_7	0.6279	1	0.4900	93° 14′
C. Orthorhombic.				
$K_2SnCl_4.2H_2O$	0.6852	1	0.7586	....
$K_2FeCl_5.H_2O$	0.6911	1	0.7178	....
D. Monoclinic.				
$MnCl_2.4H_2O$	1.1525	1	0.6445	99° 25′
$BeNa_2F_4$	0.9913	1	0.6929	99° 20′
E. Tetragonal.				
YPO_4	.	1	0.6177	.
$ZrSiO_4$		1	0.640	. .
Sn_2O_4		1	0.6726	.
F. Tetragonal.				
KIO_4		1	1.5534	....
$CaWO_4$	.	1	1.5268	....
$KOsO_3N$	.	1	1.6319	....
$KRuO_4$	.	1	1.6340	....
G. Orthorhombic.				
$KClO_4$	0.7817	1	1.2792	....
$BaSO_4$	0.8152	1	1.3136	....
KBF_4	0.7898	1	1.2830	....
H. Orthorhombic.				
K_2SO_4	0.5727	1	0.7418	....
K_2BeF_4	0.5708	1	0.7395	....
$[N(CH_3)_4]_2HgCl_4$	0.5766	1	0.7893	....
$ZnI_2.4NH_3$	0.5754	1	0.7922	....
I. Monoclinic.				
$(NH_4)_2SeO_4$	1.8900	1	1.1987	115° 29′
Cs_2HgI_4	1.3155	1	0.9260	110° 4′
(the cleavage is the same)				
J. Trigonal.				
$NaNO_3$	..	1	0.8297	....
$CaCO_3$	..	1	0.854	....
K.				
Albite $NaAlSi_3O_8$	Are closely isomorphous.			
Anorthite $CaAl_2Si_2O_8$				

The theory of chemical structure given in the recent paper in THIS JOURNAL is in full accord with these cases of isomorphism, and affords an explanation of them. In the second method[1] of regarding complex compounds with a coördination number of 6 or more, it was explained how groups such as chloride ion, ammonia, water, etc., could be held by electrostatic attraction to a positively charged central atom. We have already seen how in typical octet compounds such as potassium sulfate, etc., oxygen is unicovalent and may thus be replaced by fluorine without involving a change in the crystalline structure. The compounds in Groups A, B, G, and I are examples of this kind where fluorine, iodine or oxygen replace one another. Group C gives an illustration of a positive central ion (Sn^{++} or Fe^{+++}) surrounded by 6 other groups (Cl^- or H_2O) forming a complex ion. The H_2O group in the first compound replaces one of the chlorine ions of the second.

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[1] THIS JOURNAL, 41, 868 (1919) beginning middle of p. 930.

The compounds of Groups D and H afford interesting illustrations of the replacement of negative by positive ions and *vice versa* in a manner exactly analogous to that of Na_2O–MgF_2, etc., of Table II. Thus in $BeNaF_4$ the two sodium ions replace the two chlorine ions of the $MnCl_2.4H_2O$, the beryllium ion replaces the manganese ion and the fluorine ions replace the water comolecules. Similarly, in comparing $ZnI_2.4NH_3$ with K_2SO_4 we see that the iodide ions have replaced the potassium ions. This is evident if we apply the octet theory in the ordinary way to the compound $ZnI_2.4NH_3$. The number of available electrons in the atoms of this compound is $e = 48$. We place $n = 7$, assuming that the zinc, iodine and nitrogen atoms all form octets. We then find from the octet equation ($2p = 8n - e$) the value $p = 4$, from which we find the structure $I_2^-[Zn(NH_3)_4]^{++}$, in which each nitrogen atom is quadricovalent and shares a single pair of electrons with the octet of the zinc atom. The constitution is thus exactly analogous to $K_2^+SO_4^{--}$, for in this case the quadricovalent sulfur atom shares a single pair of electrons with each of the oxygen atoms.

If we apply the octet theory in the same way to $BeNa_2F_4$ and $MnCl_2.4H_2O$ we place for both compounds $e = 32$, $n = 5$ and find $p = 4$. This gives the structures

$$[Mn(OH_2)_4]^{++}Cl_2^- \quad \text{and} \quad [BeF_4]^{--}Na_2^+.$$

The manganese and beryllium atoms are thus quadricovalent, the water and iron share single pairs of electrons with the central atom. In the first compound the oxygen is tercovalent. The substitution of water or ammonia for fluorine or oxygen in these compounds is analogous to the substitution of K^+ in K_2SO_4 by NH_4^+.

The same explanation apply to the other examples cited by Barker. Those shown in Group K are of interest because in silicates we usually have to deal with compounds in which no pairs of electrons are held in common between atoms. Thus in the octet equation $2p = 8n - e$ we place $p = 0$ and find $e = 8n$. In silicates, oxygen is the only element which forms octets, so n is equal to the number of oxygen atoms. This condition ($e = 8n$) is practically the only valence condition that needs to be fulfilled by silicates, and it is thus a complete statement of the valence theory for these compounds. The isomorphism of the two compounds of Group K is consistent with the octet theory since in both compounds the number of atoms is alike (13) and so is also the number of available electrons, $e = 8n = 64$.

Summary.

The octet theory of valence indicates that if compounds having the same number of atoms have also the same total number of electrons, the electrons may arrange themselves in the same manner. In this case the compounds or groups of atoms are said to be isosteric Such compounds should show remarkable similarity in physical properties, that is, in those properties which do not involve a separation of the atoms in the molecule.

Table I gives a list of various isosteres predicted by the octet theory. For example, O^{--}, F^{-}, Ne, Na^{+} and Mg^{++} are isosteric Other examples are N_2—CO—CN^{-}, CH_4—NH_4^{+}; N_3^{-}—CNO^{-}; ClO_4^{-}—SO_4^{--}—PO_4^{---}; NO_3^{-}—CO_3^{--}, etc. In cases where isosteric groups have the same electric charges (isoelectric) their properties are directly comparable, thus N_2 and CO; N_2O and CO_2, KN_3 and KNCO, etc, are nearly alike (in pairs) in all their physical properties But when the charges are unlike the similarity may manifest itself between properly chosen compounds, thus, according to the octet theory, we should expect sodium nitrate and calcium carbonate to have similar constitutions and therefore to have similar crystalline forms, as is in fact known to be the case

The following cases of crystalline isomorphism are thus predicted by the theory and are found to exist according to published crystallographic data: NaF — MgO; KN_3 — KNCO, KNO_3 — $SrCO_3$; $KClO_4$ — $SrSO_4$; $NaHSO_4$ — $CaHPO_4$, $MnSeO_4.2H_2O$ — $FeAsO_4$ $2H_2O$, etc. The following cases are predicted by the theory but cannot yet be tested because of lack of available data MgF_2 — Na_2O, K_2S — $CaCl_2$, $NaClO_3$ — $CaSO_3$; $KHSO_3$ — $SrHPO_3$; $Na_2S_2O_6$ — $Ca_2P_2O_6$, $Na_2S_2O_7$ — $Ca_2P_2O_7$, etc.

The theory of isosterism makes it possible to derive certain relationships in a very simple manner. Thus since argon is an isostere of the potassium ion and methane is an isostere of the ammonium ion, it follows that the potassium and ammonium ions must have similar properties because argon and methane are nearly alike in physical properties. Similarly, the relation between argon and nitrogen enables us to trace an equally close relationship between the cyanogen and the chlorine ions. From the similarity in the solubilities of nitrates and perchlorates we may also conclude that carbonates and sulfates should be closely related.

The experimental data discussed prove that the crystalline form of substances depends on the structure as given by the octet theory, thus indicating that this theory gives a true picture of the constitutions of crystalline solids. In particular, the experimental results justify the following conclusions:

1. The covalence of sodium, potassium, chlorine in chlorides, is zero.

2. The covalence of the central atom is 4 in nitrates, carbonates, sulfates, perchlorates, phosphates, permanganates, chromates, selenates, arsenates, borofluorides, etc.

3. Carbonates and sulfites are not isomorphous, the covalence of the central atom being 4 and 3, respectively.

4. Nitrates and chlorates are not isomorphous, the covalency of the chlorine being 3 in chlorates.

5. The applicability of the octet theory to complex inorganic compounds receives further confirmation by its ability to explain such cases of isomorphism as between Na_2BeF_4 and $MnCl_2.4H_2O$; K_2SO_4 and $ZnI_2.4NH_3$, $K_2SnCl_4.2H_2O$ and $K_2FeCl_5.H_2O$, $NaAlSi_3O_8$ and $CaAl_2Si_2O_8$, etc.

SCHENECTADY, N. Y.

[CONTRIBUTION FROM THE SHEFFIELD CHEMICAL LABORATORY OF YALE UNIVERSITY.]

A STUDY OF SIDE CHAIN OXIDATIONS WITH POTASSIUM PERMANGANATE.[1]

BY LUCIUS A. BIGELOW.

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I. Introduction. II. Discussion of the Oxidation of *o*-, *m*-, and *p*-nitrotoluene. III. Experimental and Summary.

I. Introduction.

A careful review of the chemical literature upon potassium permanganate and its reactions reveals certain fundamental facts which are important both as a summary of our knowledge of the subject to date, and as a necessary introduction to an investigation in this particular field. These facts, which have been established, may briefly be expressed as follows:

1. Potassium permanganate, in concentrated aqueous solution, when treated with caustic alkali of sufficient strength and heated, spontaneously decomposes into potassium manganate and free oxygen.[2]

2. During most permanganate oxidations more or less free oxygen is evolved, and this evolution is caused by the presence of the lower oxides of manganese, or their compounds. Spontaneous decomposition of aqueous potassium permanganate solutions, with the production of free oxygen, is always brought about by the presence of these lower oxides, but does not

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[1] This paper has been constructed from a dissertation presented by the author in 1919 to the Faculty of the Graduate School of Yale University in partial fulfilment of the requirements for the Degree of Doctor of Philosophy.—T. B. JOHNSON.

[2] Aschoff, *J. prakt. Chem.*, [1] **81**, 29 (1860); Wanklyn and Cooper, *Phil. Mag.*, [5] **7**, 138 (1879); Sackur and Taegner, *Z. Elektrochem.*, **18**, 718 (1912).

occur in their absence. The researches of Morse and his students,[1] supported by the work of many other investigators, have established these facts, although some contrary evidence has been presented.[2] The mechanism of the reactions to which the oxygen evolution is due has not been satisfactorily explained One suggestion offered is to the effect that manganese dioxide, if precipitated, polymerizes at the expense of permanganic acid, liberating the oxygen from the latter.[3]

3. The decomposition of potassium permanganate, in aqueous solution, is stimulated by an increase in concentration, or a rise in temperature.[4]

4. Benzene derivatives of various structures, even those with the same substituents, but in different positions, show wide differences in susceptibility to oxidation by potassium permanganate and other oxidizing agents; yet these phenomena show little regularity. Remsen's law,[5] which does not by any means hold in all cases, seems to be the only important generalization which has been made in this field.

5. When organic compounds are oxidized by potassium permanganate in alkaline solution, an increase in the concentration of the alkali present may produce distinctly different effects in different cases.[6]

6. Catalyzers may greatly affect permanganate reactions [7]

Insofar as I have been able to determine from the literature, no systematic attempt has been made to determine the manner in which the progressive variation of the conditions influencing the oxidation of any given series of aromatic compounds affects the products of such reactions. This applies both to the yields obtained and to the amounts of unchanged material recovered in the process. Moreover, most of the work described in the literature which in any way bears upon the subject, has been carried out with relatively very small quantities of material. It has been my object, in this investigation, to select a definite series of aromatic compounds, with an aliphatic side chain, and to submit this side chain to oxidation by potassium permanganate, in alkaline solution, in such a manner as to make possible a study of the influence of conditions upon the reactions. There have been taken into consideration not only the quantity and rate of addition of the oxidizing agent, but also the alkalinity of the oxidizing mixtures, the concentration and temperature of the solutions, and the influence of certain catalyzers. The work has been carried out on a moderately large laboratory scale, and it is hoped that the results may be of some value in the practical application of potassium permanganate as an oxidizing agent.

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[1] Morse, Hopkins and Walker, *Am. Chem J*, 18, 401 (1896); Morse and Reese, *Ibid.*, 20, 521 (1898); Morse and Byers, *Ibid.*, 23, 313 (1900); Brand and Ramsbottom, *J. prakt. Chem.*, [2] 82, 382 (1910); Gooch and Danner, *Am. J. Sci*, [3] 44, 301 (1892).

[2] Meyer and von Recklinghauser, *Ber.*, 29, 2549 (1896); Hirtz and Meyer, *Ibid.*, 29, 2828 (1896).

[3] Morse and Byers, *Am. Chem. J.*, 23, 313 (1900).

[4] Brand and Ramsbottom, *J. prakt. Chem.*, [2] 82, 382 (1910); Morse and Reese, *Am. Chem. J.*, 20, 521 (1898).

[5] Remsen, *Am. Chem. J.*, 1, 36 (1879); Remsen and Palmer, *Ibid.*, 4, 142 (1882); Richard Meyer, *Ann.*, 220, 16 (1883).

[6] Behrend, *Ann.*, 333, 159 (1904); Witzemann, This Journal, 38, 150 (1916); Evans and Day, *Ibid.*, 38, 375 (1916).

[7] Doroschevski and Pavlov, *J. Chem. Soc.*, [2] 110, 24 (1916).

II. Discussion of the Oxidation of *o*-, *m*- and *p*-Nitrotoluenes.

For this work the 3 nitrotoluenes were selected as representative examples of aromatic side chain compounds to be submitted to oxidation by potassium permanganate. They were chosen for 3 reasons: (1) They are available in quantity, and each of them undergoes oxidation readily to the corresponding acid. (2) They constitute a typical series of disubstituted benzene derivatives, hence a study of their relative properties might throw some further light upon the benzene problem. (3) Two of the products of oxidation, *o*-, and *p*-nitrobenzoic acids, are of possible technical value; the former in the synthesis of dyes, and the latter in the manufacture of pharmaceuticals.

While the *o*- and *p*-nitrotoluenes can readily be purchased upon the market, the *m*-compound was not available in this way, and had to be synthesized in the laboratory. The only synthesis already described which seemed suitable for this purpose was that starting from *m*-nitro-*p*-toluidine, $C_6H_3(CH_3)(NO_2)(NH_2)$, which is converted into *m*-nitrotoluene by diazotization and reduction, substituting the amino group by hydrogen. The nitrotoluidine is best prepared from commercial *p*-toluidine, by acetylation, nitration, and subsequent saponification. All these reactions have been carefully studied, with the idea of establishing the best conditions under which they may be carried out, in order to obtain good yields with a minimum quantity of reagents and the smallest expenditure of time and effort. It has been found possible to effect the nitration by means of a small quantity of a "mixed acid" consisting of ordinary conc. nitric and sulfuric acids, while the diazotization and reduction take place much more smoothly in the presence of a small amount of copper powder, which acts as a catalytic agent. A practical laboratory method for carrying out the synthesis is described in the Experimental Part.

The oxidation of the nitrotoluenes, the study of which constitutes the main problem under investigation, was entirely carried out in alkaline or nearly neutral solutions. The plan has been not so much to attain the highest possible purity of product upon a very small scale, as to make a product of high commercial quality in relatively large quantities. The reactions have been studied from the point of view of the investigator who desires to synthesize considerable amounts of material, or to acquire data of value in a commercial application of the reactions involved.

It has been found that every influence that has been studied, which can be brought to bear upon the oxidation of the nitrotoluenes with alkaline potassium permanganate, has a marked effect upon the results obtained. While it might naturally be expected that entirely different kinds of changes in the conditions of oxidation would produce widely different types of changes in the results, this is not the case. Whatever change of conditions was made, it was found, in general, that the result was merely to cause a *different proportion* of the nitrotoluene present to be attacked by the oxidizing agent. The yield in grams of nitrobenzoic acid is altered, but the weight of unchanged nitrotoluene recovered is also altered, in the inverse direction, and in such a manner that the sum of the two remains not far from a *constant quantity*. This holds true to a striking extent, notwithstanding the fact that certain changes of procedure do cause the "constant," as well as the quality of the product, to vary somewhat.

These facts plainly enable us to draw two important conclusions with regard to the oxidations, as follows. First, the quantity of nitrotoluene, or of nitrobenzoic acid, entirely destroyed by the oxidizing agent, is essentially constant for each nitrotoluene, and is not greatly affected by changes in the oxidation procedure. Second, inasmuch as the permanganater, usually present in excess, is in all cases entirely reduced, at least *two entirely independent changes* take place at the same time in the reacting mixture, namely, the oxidation of the organic compound, and the decomposition of the permanganate into manganese oxides and free oxygen. The effect of altering the conditions or procedure is thus either to *accelerate* or to *retard one* or the *other* of these changes, which will cause a greater or less proportion of the nitrotoluene to be converted into the corresponding acid *before* the whole of the permanganate present has been reduced. It has been well established that permanganate is nearly always decomposed with the evolution of oxygen when in the presence of any of the oxides of manganese, and these must of necessity be present in the alkaline reacting mixture as soon as any of the permanganate has been reduced by the organic matter present. It has been shown, however, that if a solution containing alkali and permanganate, in the proportions most frequently employed in this work, is boiled for a prolonged period, no decrease in its oxidizing power can be detected provided it contains no organic matter, and no suspended oxides of manganese

Turning now to a consideration of the influence upon the reaction of the specific changes of conditions which have been studied, it is found that increasing the concentration of alkali in the oxidizing mixture up to a certain point *favors* the oxidation of *o*-nitrotoluene, beyond which point a further increase produces essentially no effect, all other conditions being kept constant. By this increase in alkaline concentration the oxidation of the *meta* compound is *hindered*, such oxidation being most effective in an essentially neutral medium; while that of the *para* isomer is *favored* up to a certain point, beyond which the quality of the product becomes very poor. In all probability, then, the presence of alkali on the one hand accelerates considerably the oxidation of the *o*- and *p*-nitrotoluene, and does not so much affect that of the *m*-nitrotoluene; while on the other hand it accelerates to a certain extent the decomposition of the permanganate It is plain that if the alkali accelerates the oxidation of the *o*- and the *p*-nitrotoluenes more than it does the decomposition of the permanganate, the oxidation of these compounds will be favored by increasing concentrations of alkali, while if the oxidation of the *meta* isomer is not accelerated as much as the decomposition of the oxidizing agent, the oxidation of this derivative will be hindered by the presence of alkali.

The fact that the oxidation of the *o*- and *p*-compounds is so much more accelerated by the alkali than that of the *m*-compound, suggests to the writer that this difference in behavior is due to the difference in molecular construction of the 3 isomers. It is well known that aromatic combinations which can assume a quinoid structure are more susceptible to chemical attack than those which must retain the benzenoid form. Theoretically, especially in the presence of alkali, both *o*- and *p*-nitrotoluene can assume a quinoid structure, while no such configuration can be assigned to the *m*-compound. Consequently it seems logical to assume that the difference in chemical behavior may be due to these tautomeric changes.

Again, there is some evidence in the literature[1] to the effect that the presence of alkali in a solution in which potassium permanganate is reduced affects the physical state of the oxides of manganese precipitated. It is known that these oxides are very active in inducing the decomposition of permanganate, so that it seems reasonable to assume that the concentration of alkali, in our oxidations, might affect the rate of decomposition of the oxidizing agent In all cases it has been found that alkali increases the rate of reaction. This is in accord with the assumptions which have been made regarding the quinoid structure in the cases of the *o*- and *p*-nitrotoluenes, and the increased rate of decomposition of the permanganate in the case of the *m*-isomer.

An increasing dilution of the reaction mixture favors the oxidation of all the nitrotoluenes, which is quite what would be expected from the statement in the literature that an increasing concentration of a permanganate solution stimulates the decomposition of the permanganate into manganese oxides and free oxygen. Highly concentrated, alkaline oxidation mixtures very rapidly become deep green, indicating the decompostition of the permanganate directly into manganate and free oxygen. It was found in the oxidation of the *p*-nitrotoluene that an increasing quantity of permanganate in excess of the theoretical quantity favors the reaction up to a 10% excess, but not beyond this. A greater quantity of permanganate merely oxidizes nitrotoluene without increasing the yield of nitrobenzoic acid. The 10% excess also seems to give a better quality of product, and was arbitrarily adopted in the oxidation of the other nitrotoluenes. While most of the oxidations described in this investigation were carried out at the boiling temperature of the reacting mixture, the influence of lowering the temperature was studied in the case of the *p*-nitrotoluene. The yield obtained was considerably decreased, and the time of oxidation greatly increased by this procedure. This shows that while lowering the temperature decreases the rate of decomposition of the permanganate into manganese oxides and free oxygen, it decreases the rate of oxidation of the *p*-nitrotoluene to an even greater extent.

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[1] Jones, *J. Chem. Soc.*, 33, 95 (1878).

Catalytic influences upon the reaction have been studied in the oxidation of *o*- and *p*-nitrotoluenes, by carrying these out in 3 different types of container, one of iron, one of copper, and one lined with enamel, which is the equivalent of one of glass. It was found that in both cases nearly the same results were obtained in the copper and the enamel lined containers; but distinctly lower yields, and products of poorer quality, in the iron container, both with and without alkali. Evidently the metallic iron catalyzes the decomposition of permanganate. The addition of salts of calcium and magnesium to the reaction mixture in the oxidation of *p*-nitrotoluene in neutral solution produced no noticeable effect; nor did the addition of pyridine to a similar oxidation in alkaline solution, although it acts as a strong negative catalyst in certain permanganate reactions.[1]

Considering the results from the point of view of position in the benzene ring, it has been shown that *p*-nitrotoluene under all conditions is oxidized most readily, the *o*-compound next, and the *m*-isomer least. There seem to be no valid generalizations in the literature upon the relative rates of oxidation of *o*-, *m*-, and *p*-compounds to which these results may be compared intelligently. It appears, however, to be in accord with general experience, that the *o*-compound should oxidize somewhat more slowly than the *p*-isomer, on account of the protective influence of the strongly negative nitro group in the *o*-position to the methyl group (Remsen's law). Why the *m*-isomer should be so resistant to oxidation is quite obscure as yet, although there are some recorded cases[2] in which *m*-disubstituted benzene derivatives show this property. As far as my work has extended, all changes of the conditions of oxidation except one, affect the 3 isomers in the same general way. The exception is the influence of alkali, which, as has already been described, stimulates the oxidation of the *o*- and *p*-nitrotoluenes, but retards that of the *m*-derivative.

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[1] Michael and Garner, *Am. Chem. J.*, 35, 267 (1906).

[2] Bruckner, *Ber.*, 9, 406 (1876); Renter, *Ibid.*, 17, 2028 (1894).

III. Experimental Part.

The Preparation of Meta-nitrotoluene.

All the nitrotoluene employed in this research was prepared in the laboratory from *p*-toluidine. This base was first converted into its acetyl derivative by digestion with glacial acetic acid and the acetate then subjected to nitration[1] with a mixture of sulfuric and nitric acids. It was found that it was unnecessary to use fuming nitric acid for this operation, and the results of several preliminary experiments showed that the best yields are obtained by nitrating at a temperature of 30 to 40°. The results of a series of nitrations with different proportions of acids are recorded in the table below

TABLE I

Nitrations with Different Proportions of Acids

20 g. of acetotoluide used in each experiment.

Expt.	Sulfuric acid (S. G. 1.84) Cc.	Nitric acid Cc.	Nitric acid Mols.	Yield of nitrotoluide. %	M. P. Degrees.	Character of the product.
1	20	68	8	85	93–4	Good
2	20	59.5	7	85	92–4	Good
3	20	51	6	85	91–2	Not so pure
4	40	42.5	5	77	80–	Impure
5	20	42.5	5	88	88–92	Not very pure
6	10	42.5	5	77	88–93	Fairly good
7	7.5	34	4	78	94–6	Good
8	7.5	25.5	3	78	93–4	Good
9	7.5	22.5	2.6	79	94–5	Good
10	0	22.5	2.6	67	75–90	Very impure
11	7.5	17	2	73	90–4	Good
12	5.0	17	2	62	92–4	Good

It will be observed that the proportions represented in Expts. 8 and 9 are productive of the maximum yield of *m*-nitro-*p*-acetotoluide, $C_6H_3(CH_3)(NO_2)^3(NH.COCH_3)^4$ for a low molecular concentration of nitric acid. The proportions represented in Expt. 8 were finally adopted as most advantageous on the whole, and were used in all nitrations upon a large scale. The product so obtained is of good quality, and the yield of the toluide, 78% of the theoretical, is quite satisfactory. A "mixed acid" made up in the following proportions gives good results: Nitric, 50%; sulfuric, 25%; and water, 25%. Twenty g. of *p*-acetotoluide requires 50.5 g. of this mixture. It has been my experience that this nitration proceeds very quickly and that it is not necessary to let the mixture stand longer than 15 minutes after final addition of the acetotoluide to the mixed acids.

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[1] Beilstein and Kuhlberg, *Ann.*, 155, 24 (1870); Gattermann, *Ber.*, 18, 1482 (1885); Nolting and Collin, *Ibid.*, 17, 264 (1884). Noyes, *Am. Chem. J.*, 10, 475 (1888); Reverdin and Le Duc, *Ber.*, 43, 3460 (1910).

The acetyl derivative was hydrolyzed in the usual manner by digestion in alcohol with sodium hydroxide[1] and the nitrotoluidine then subjected to diazotization and reduction with alcohol in order to replace the amino group with hydrogen.[2] A greater or less excess of sodium nitrite had but little effect upon the yield of nitrotoluene produced, and an excess of 20% was adopted as most convenient. I introduced one modification in Buchka's method, namely, the incorporation of copper powder to catalyze the reduction reaction. Although this metal has been used by several investigators, among whom may be mentioned Tobias,[3] St. Von Niementowski,[4] Ullmann and Bieleck[5] to catalyze the evolution of nitrogen from diazo compounds and to effect condensations, there does not seem to appear in the literature any description of its use in a process where reduction of a diazo group with alcohol is applied. I found that the yields of nitrotoluene could be greatly increased by use of the metal, and in the following table are recorded the results of a series of experiments showing its effect.

TABLE II.

Effect of Copper Powder on the Diazotization

Weight of *m*-Nitro-*p*-toluidine in Each Case, 25 g. Time of Standing after Diazotization; 3 Hours

Expt	95% alcohol Cc	Sulfuric acid (conc.) Cc	Nitrite solution 100 g NaNO$_2$ in 165 cc H$_2$O Cc	Copper powder G	Yield of *m* nitro toluene %	Remarks
1	95	14	22.5	2	73	
2	95	14	22.5	2	72	Catalyzer added before diazotization
3	95	14	22.5	0	59	Much tar
4	95	14	22.5	12.5	73	Little tar
5	63	14	22.5	2	63	
6	143	14	22.5	2	53	
7	95	14	22.5	2	67	
8	95	55 HCl sp. gr. 1.20	33.8	2	82	Product contained chlorine

It has been my experience that the alcohol recovered from a reduction process cannot be used again successfully as the aldehyde impurity interferes with the reaction. Attempts to reduce the diazo compound with stannous chloride in hydrochloric acid solution, or with sodium stannite in alkaline solution were unsuccessful. The exact procedure for carrying out the preparation of nitrotoluene from *m*-nitro-*p*-toluidine may now be summarized as follows:

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[1] Gatterman, *Loc. cit.*; Noyes, *Ibid.*

[2] Buchka, *Ber.*, 22, 829 (1889).

[3] *Ber.*, 23, 1628 (1890).

[4] *Ibid.*, 34, 3325 (1901).

[5] *Ibid.*, 34, 2174 (1901).

100 g. of *m*-nitro-*p*-toluidine is added to a mixture of 375 cc. of 95% alcohol and 56 cc. of sulfuric acid, sp. gr. 1.84. The mixture is heated until solution is complete, cooled in ice water, and vigorously stirred. 90 cc. of a solution of sodium nitrite, containing 100 g. of sodium nitrate in 165 cc. of solution, is allowed to flow in, drop by drop, during a period of about 20 minutes. The reaction mixture is allowed to stand in the cold for 3 hours. 8 g. of copper powder is next added, in portions, and the flask placed in cold water. The mixture gradually warms to about 40°, and the nitrogen is promptly and rapidly evolved. The alcohol is then distilled off, the residue steam distilled and extracted with ether. After the removal of the ether the crude *m*-nitrotoluene is heated to its boiling point to expel the last traces of ether and is obtained as a red oil weighing about 66 g., equivalent to 73% of the theoretical yield. The crude product is purified by distillation. With the apparatus at my disposal, its boiling point was found to be 110° at 15 mm., 113–14° at 18 mm., 128° at 32 mm.; and 223° at ordinary pressure, "uncorrected." According to the literature, *m*-nitrotoluene boils at 228–231° ("uncorrected?") and melts at 16°.

The Oxidation of the Nitrotoluenes with Potassium Permanganate.

The oxidation of the 3 nitrotoluenes to the corresponding nitrobenzoic acids has long been known, and has been carried out by numerous investigators. The oxidizing agents used by them for this purpose, notably potassium dichromate in sulfuric acid solution, and potassium permanganate in alkaline solution, have been very frequently applied, both in these and many other similar oxidations. A careful search of the literature, however, has failed to reveal any comparative series of oxidations similar to that described in the following pages. A summary of the numerous isolated examples which are recorded is not necessary at this point.

The *o*-nitrotoluene submitted to oxidation was purchased in the market. It was quite pure, boiling mostly from 213 to 218°, the true boiling point being 218°,[1] and was not further purified. The *m*-nitrotoluene was synthesized as already described, and the purified product employed in the oxidation experiments. The *p*-nitrotoluene was purchased upon the market. It melted at 54–6°, the true melting point being 54°,[2] and it was used directly in the subsequent work. The potassium permanganate employed as the oxidizing agent was the usual commercial product. Two large lots which were received at the laboratory were analyzed to determine their oxidizing power with the following results:

Lot A. 1 g. $KMnO_4 \rightleftharpoons 1.974, 1.970$ g. $H_2C_2O_4.2H_2O$

Calc., 1 g. $KMnO_4 \rightleftharpoons 1.993$ g. $H_2C_2O_4.2H_2O$.

Lot B. 1 g. $KMnO_4 \rightleftharpoons 2.207, 2.212$ g. $(NH_4)_2C_2O_4.H_2O$

Calc., 1 g. $KMnO_4 \rightleftharpoons 2.247$ g. $(NH_4)_2C_2O_4.H_2O$.

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[1] *Ber.*, 24, 1987 (1891).

[2] *Z. Chem.*, *N. F.*, 1, 220 (1865).

Therefore, the oxidizing power of the permanganate was 98.9, 98.4% of the theoretical value. As this potassium permanagnate was very nearly pure, at least with regard to its oxidizing power, it was used directly as the oxidizing agent. The sodium hydroxide used was the usual high grade commercial product, and the solvent employed was water.

The only part of the apparatus required in the process which merits any detailed description is the container in which the oxidation took place. In order to determine the catalytic effects of 3 different metals upon the reactions, 3 different types of container were used. They were a copper kettle, an enamel lined iron pot, and an iron drum. The copper kettle was made especially for this investigation. The enamel lined pot had been used for various purposes for some time, but although it was somewhat corroded, the enamel nevertheless covered almost all the surface of the iron. The iron drum was of the ordinary commercial variety, and was subjected to an extremely thorough cleaning before it was used in this work.

The general method employed in carrying out the oxidations was essentially the same in all cases, and was, in detail, as follows.

The water was first measured into the container, and the desired quantity, if any, of sodium hydroxide weighed out and added to it. Next the nitrotoluene was carefully weighed out—in the majority of cases accurately to 0.1 g.—and poured into the sodium hydroxide solution. The container was then fitted with an inclined reflux condenser, and the contents heated nearly to boiling. In the meantime the potassium permanganate to be used was weighed and divided into a number of approximately equal parts, the first of which was added in the solid state to the hot alkaline solution containing the nitrotoluene in suspension. The mixture was finally heated to boiling. When the pink color imparted to the solution by the permanganate had disappeared, the next portion was added, and so on until all had been used up. The product was then distilled with steam, to recover the unchanged nitrotoluene. The steam distillate was extracted with ether, the ether solution dried, and the ether removed in the usual way. After the ether had distilled off the residue was heated for a time on the boiling water bath, to expel the last traces, and then cooled and weighed. The main solution was washed out of the container, evaporated over a free flame to a convenient volume, and filtered from the precipitated oxides of manganese. The filtrate was then further evaporated, and filtered again to remove the traces of manganese oxides which nearly always passed through the filter in the colloidal condition the first time. The filtrate, which was usually yellow in color and contained sodium nitrobenzoate, was finally further concentrated and acidified hot, with conc. hydrochloric acid. After cooling the solution, the nitrobenzoic acid which was deposited was filtered off, dried and weighed. It was not further purified.

In the oxidation of *o*-nitrotoluene, a 25 g. sample was used, but the results have all been calculated on the basis of a 50-g. sample for the sake of uniformity. The time in general required to decolorize one portion of the permanganate varied from half an hour to an hour, depending upon the proportion of alkali present. In all cases, the presence of alkali in the oxidation mixture increased the velocity of the reaction. The sodium *o*-nitrobenzoate solutions were light yellow in color, but of a progressively deeper shade as the alkalinity of the oxidation mixture increased. The *o*-nitrobenzoic acid always separated in the crystalline condition, the color of the product varying from almost pure white to distinctly yellow, following, in general, the color of the solution from which it separated. The solubility determinations of Oechsner de Coninck[1] show that a saturated solution of *o*-nitrobenzoic acid in dil. hydrochloric acid contains somewhat over 2 g. of the former in 500 cc., at 8.5°. The solutions were, therefore, evaporated to approximately that volume before precipitation, and cooled to 8 or 9° before filtration. Two g. was then added to the weight of acid obtained in order to get the true yield. The product was in every case nearly pure *o*-nitrobenzoic acid. It melted at 139–42°, but sintered at a slightly lower temperature. The melting points given in the literature are 141°,[2] 145°,[3] 147°.[4]

The *m*-nitrotoluene was also oxidized in 25 g. samples, but the results calculated on the basis of a 50-g. sample. The oxidation was at only a little slower rate than that shown by the *ortho* compound. It was accelerated by the presence of alkali. The color of the solutions and that of the product, which invariably separated in the crystalline condition, varied from white to yellow, depending upon the proportion of alkali present, as in the case of the *ortho* compound. Following the solubility determinations of de Coninck, the solutions were evaporated to 500 cc., cooled to 20° and 1.5 g. added to the weight of acid obtained in each oxidation, to allow for the quantity remaining in the mother liquors. The *m*-nitrobenzoic acid melted at 136–8° and was a satisfactory product. The melting point is given in the literature as 140–1°.[5]

The *p*-nitrotoluene was oxidized in 50-g. samples. Inasmuch as it is a solid at ordinary temperatures, the extraction of the steam distillate with ether was unnecessary. The unchanged material was filtered off, dried at a low temperature, and weighed. The speed of oxidation of the *para* compound was always essentially twice as great as that of the *ortho* isomer, and, furthermore, was twice as great in an alkaline as in a neutral

[1] *Compt. rend.*, 118, 538 (1894).
[2] *Ann.*, 163, 135 (1872).
[3] *Ibid.*, 166, 133 (1873).
[4] *Ibid.*, 193, 221 (1878).
[5] *Ibid.*, 193, 213 (1878).

solution. Thus it required, in an alkaline medium, only about 15 minutes to decolorize one portion of the permanganate. The alkaline solutions of sodium *p*-nitrobenzoate varied in color all the way from very light yellow to dark red, and the precipitated product was either amorphous or crystalline, depending chiefly upon the quantity of alkali present during the oxidation. The amorphous variety varied in color from reddish brown through brown to light gray, while the crystalline modification varied from light brown through pink to almost pure white. As *p*-nitrobenzoic acid is exceedingly insoluble in water, the solutions were not evaporated to a volume much less than one liter, and no correction was applied for the acid remaining in the mother liquors. The solutions were filtered cold. The products in nearly all cases melted at 234–7°—a few at about 230°. The true melting point of *p*-nitrobenzoic acid is given as 238°.[1]

In all the oxidations, the products having the best appearance, which were crystalline, and white or nearly so, were obtained from neutral oxidation mixtures, but such products were no more pure than the rest, as shown by their melting points. In cases where the percentage concentration of the alkali in the solution was high, the pink color of the permanganate very rapidly gave place to a deep green. If the alkali concentration was low no green color whatever was produced. Lastly, the oxides of manganese precipitated in a neutral oxidation were darker and denser than those which were formed in the presence of alkali.

The Oxidation of *o*-Nitrotoluene, $C_6H_4(CH_3)^1(NO_2)^2$. – The first study made in the oxidation of *o*-nitrotoluene was that of the influence of a varying concentration of alkali upon the reaction. The quantity of permanganate used, 128 g., was 10% in excess of the calculated amount, which is 116 g. for a 50-g. sample. This excess had previously been found most advantageous in the oxidation of *p*-nitrotoluene. The results obtained are summarized in the following table.

TABLE III.

(Oxidations of *o*-Nitrotoluene in the Copper Containers.)

50 g. of *o*-Nitrotoluene, 128 g. of Potassium Permanganate and 3150 cc. of Water Used in Each Experiment

Expt.	NaOH G.	Unchanged *o*-nitrotoluene G.	Yield of *o*-nitrobenzoic acid G.	Yield + unchanged G.
1	0	12.0	38.0	50
2	4	9.8	37.0	47
3	[illegible]	8.6	38.8	47
4	16	7.2	40.8	48
5	32	6.2	41.0	47
6	64	6.2	44.6	51
7	84	4.6	45.2	50
8	104	5.2	44.6	50
9	128	4.8	45.4	50

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[1] *Ann.*, 193, 226 (1878).

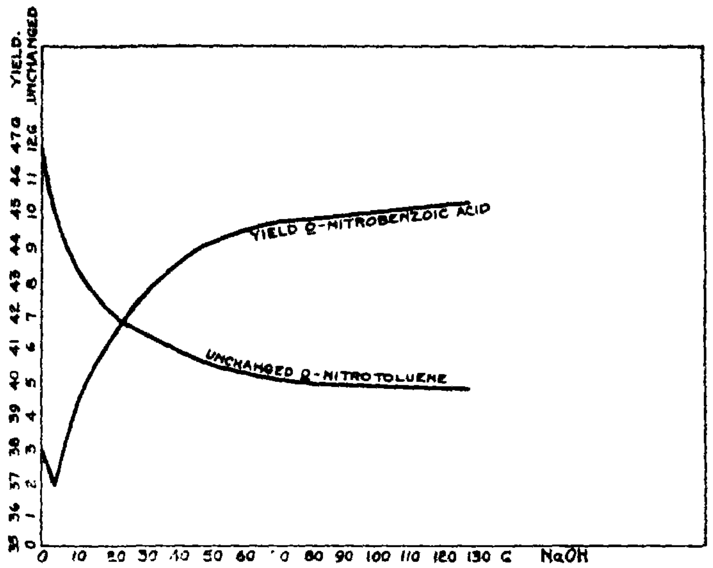

Fig 1 *o* Nitrobenzoic acid produced and *o* nitrotoluene recovered *vs* alkali

The results show that an increasing percentage concentration of the alkali in the solution favors the oxidation of *o*-nitrotoluene up to a certain point, but beyond that has but little effect Expt. 6 represents the most favorable concentration.

Next a study of the influence of dilution upon the oxidation was made, both with and without the optimum concentration of alkali. The results are recorded below

TABLE IV

Effect of Dilution

Oxidations in the Copper Container

50 g of *o*-Nitrotoluene and 128 g of Potassium Permanganate Used in Each Experiment.

Expt	Portions of $KMnO_4$	Water Cc	NaOH G	Unchanged o-nitro-toluene G	Yield of o-nitrobenzoic acid G	Yield + unchanged G
1	8	500	64	29.4	9.4	39
2	8	1575	64	10.2	37.6	48
3	4	3150	64	6.2	44.6	51
4	2	6300	64	5.4	49.8	55
5	8	500	0	23.6	18.8	42
6	8	1575	0	13.4	31.4	45
7	4	3150	0	12.0	38.0	50

In the absence of alkali, the time required to decolorize $^1/_8$ of the permanganate was as high as 1.5 hours. The results show that both with and without alkali, increasing dilution very greatly favors the oxidation.

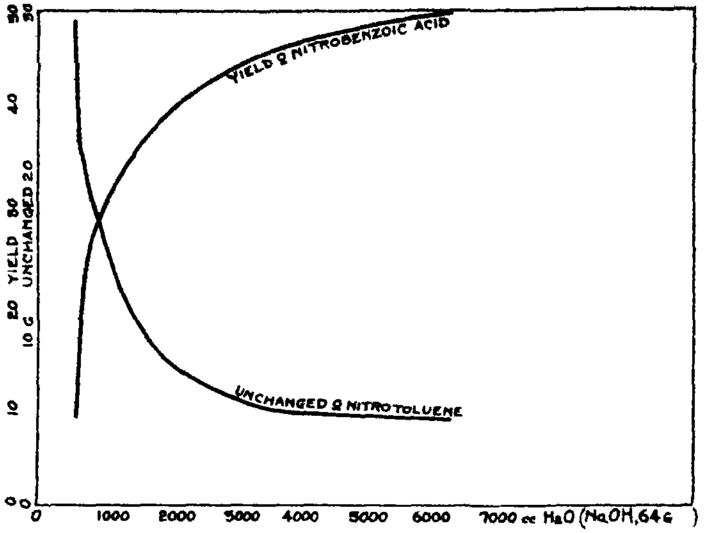

Fig. 2.—*o*-Nitrobenzoic acid produced and *o*-nitrotoluene recovered *vs.* dilution.

A study of the catalytic effect of the container upon the oxidation was now carried out with the following results:

Table V.

Catalytic Effect of the Container.

50 g. of *o*-Nitrotoluene, 128 g of Potassium Permanganate in 4 Portions, and 3150 cc. of Water Used in Each Experiment.

Expt.	NaOH. G	Unchanged *o*-nitrotoluene G.	Yield of *o* nitrobenzoic acid G	Unchanged + yield G	Container used.
1	64	14.0	36.0	50	Iron
2	64	6.2	44.6	51	Copper
3	64	7.0	44.0	51	Enamel
4	64	8.2	42.8	51	Enamel
5	0	14.0	32.0	46	Iron
6		12.0	38.0	50	Copper
7	0	14.0	36.0	50	Enamel

Here it is seen that both with and without alkali, the oxidations performed in the copper and enamel containers gave essentially the same results, while those carried out in the iron drum gave a lower yield. They also gave a more highly colored product.

The best conditions found for oxidizing *o*-nitrotoluene to *o*-nitrobenzoic acid are those represented in Expt. 2, Table V. The product obtained is satisfactory, and the yield is 73% of the theoretical amount. If the unchanged nitrotoluene recovered is allowed for, the yield becomes 84% of the calculated amount. The yield obtained in Expt. 4, Table IV, is considerably higher, but the dilution is so great that it is not practical to employ the proportions there used.

The Oxidation of *m*-Nitrotoluene, $C_6H_4(CH_3)^1(NO_2)^3$.—The reagents, apparatus, methods of operation and general considerations have already been described.

The influence of alkali upon the oxidation was first studied, and the results obtained, which were quite unexpected, are summarized below:

TABLE VI.

Influence of Alkali

Oxidations in the Copper Container.

50 g. of *m*-Nitrotoluene, 128 g. of Potassium Permanganate in 4 Portions and 3150 cc. of Water Used in Each Experiment.

Expt.	NaOH. G	Unchanged *m*-nitrotoluene. G	Yield of *m*-nitrobenzoic acid G	Unchanged + yield. G.
1	0	20 2	27 1	47
2	4	19 6	27 3	47
3	8	20.6	25 9	47
4	16	20 8	24 9	46
5	32	22.4	22.7	45
6	64	25.2	18 9	44
7	84	26.8	17.7	45
8	104	28 0	16 5	45
9	128	28 4	16.1	45

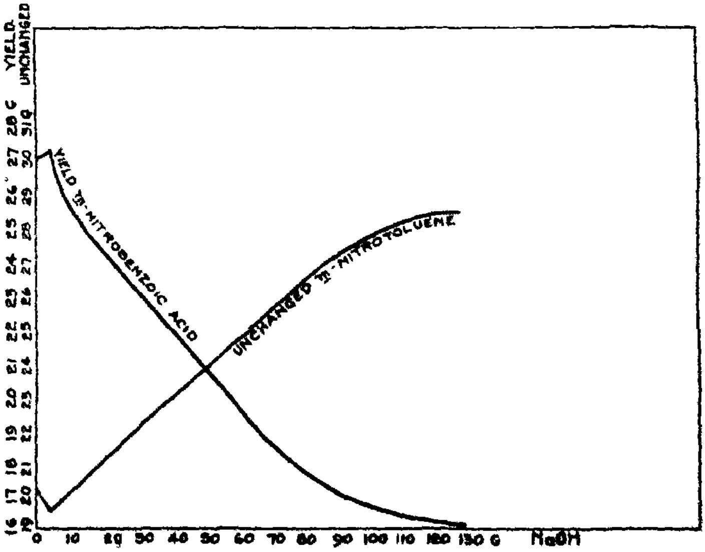

Fig. 3.—*m*-Nitrobenzoic acid produced and *m*-nitrotoluene recovered *vs.* alkali.

The results show that in this case the effect of the alkali is just the reverse of what it is in the oxidation of the *ortho* compound, as here an increase in the percentage concentration of the alkali in the oxidizing mixture *hinders* the oxidation, which is most efficient in an essentially *neutral* medium.

The influence of various degrees of dilution upon the reaction is shown by the following summary:

TABLE VII.

Influence of Various Degrees of Dilution

Oxidations in the Copper Container

50 g. of *m*-Nitrotoluene and 128 g. of Potassium Permanganate Used in Each Experiment

Expt.	Portions of $KMnO_4$.	Water. Cc	NaOH G	Unchanged *m* nitrotoluene G	Yield of *m*-nitrobenzoic acid G	Unchanged + yield G.
1.	8	500	0	32.0	8.7	41
2		1000	0	25.2	14.7	40
3	8	1575	0	23.4	19.1	43
4 .	4	3150	0	20.2	27.1	47
5 ..	2	6300	0	17.2	32.3	50

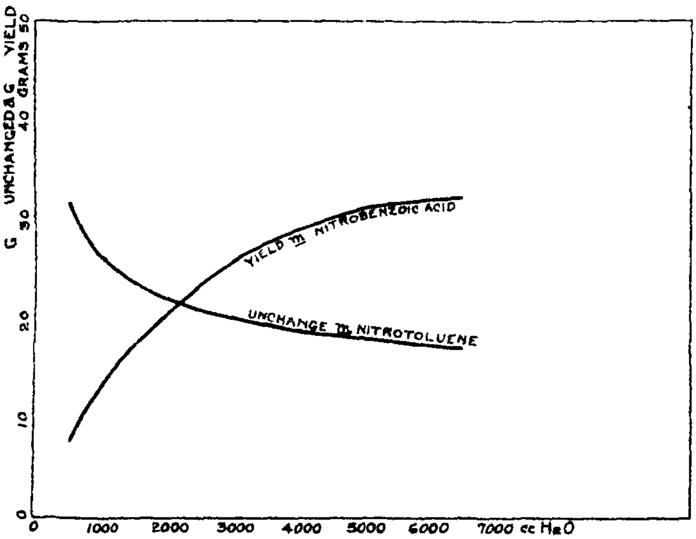

Fig 4.—*m*-Nitrobenzoic acid produced and *m* nitrotoluene recovered *vs* dilution

These results indicate that the oxidation of the *m*-nitrotoluene, in common with that of the *ortho* compound is greatly favored by increasing dilution of the solution.

The most advantageous conditions for the oxidation of *m*-nitrotoluene are on the whole represented in Expt. 1, Table VI. The product is of good quality, and the yield is 44% of the theoretical. If allowance is made for the unchanged nitrotoluene recovered, the yield is raised to 74% of the calculated amount. As in the case of the *ortho* compound, a higher dilution improves the yield (Expt. 5, Table VII), but is hardly practical for general use.

To determine whether or not the potassium permanganate was decomposing spontaneously in the boiling solutions, 16.0 g. of permanganate, 1575 cc. of water, and 32 g. of sodium hydroxide were placed in the copper kettle, and the mixture boiled for about 8 hours. Before boiling the solution, an aliquot part was taken out and titrated against a standard solution of ammonium oxalate, containing 0.0100 g. per cc. After boiling the solution, another aliquot part was taken out and titrated in a similar manner It oxidized an amount of oxalate identical with the first. Therefore, the oxidizing power of the potassium permanganate solution was not decreased by boiling it for 8 hours in an alkaline solution of a strength equal to that employed in the oxidation experiments which gave the best results.

To this permanganate solution was next added 2.5 g *m*-nitrotoluene, and the boiling resumed. A partial reduction of the permanganate took place immediately, but the last of the pink color of the solution disappeared very gradually, about 7 hours of boiling being required to decolorize the mixture entirely. The resulting solution was worked up in the usual manner. There was recovered 0.4 g. of unchanged nitrotoluene, and the yield of *m*-nitrobenzoic acid produced was 2.1 g. (= 0.6 + 1.5).

This indicates that a small amount of the *m*-nitrobenzoic acid had been burned up, and that the presence of the organic matter in the solution did not catalyze the decomposition of the permanganate to any very significant extent.

The Oxidation of *p*-Nitrotoluene, $C_6H_4(CH_3)^1(NO_2)^4$.—The oxidation of the *p*-nitrotoluene was investigated much more fully than that of either of the other two isomers; and some of the relative proportions of the reagents involved which were adopted in the oxidations of the other nitrotoluenes, were derived from the results of the work upon the *para* compound. The reagents, the apparatus, and the general method are described above. The oxidizing mixture first used was approximately that suggested by Noyes[1] the quantity of permanganate employed being the calculated amount.

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[1] "Organic Chemistry for the Laboratory," 1897, p. 26. Chem. Pub. Co., Easton, Pa.

The first study made was, as usual, upon the influence of alkali upon the oxidation, and the results obtained are expressed in the table below:

TABLE VIII.

Influence of Alkali.

Oxidations in the Enamel-lined Container.

50 g. of *p*-Nitrotoluene, 116 g. of Potassium Permanganate in 5 Portions and 1575 cc. of Water Used in Each Experiment.

Expt.	NaOH. G.	Unchanged *p*-nitrotoluene. G	Yield of *p*-nitrobenzoic acid G	Unchanged + yield. G	Character of product.
1........	4	15	32	47	Amorphous
2.	8	12	34	46	Amorphous
3........	16	12	36	48	Amorphous
4........	32	8	39	47	Amorphous
5.	64	9	39[1]	48	Amorphous
6........	128	5	42	47	Reddish and amorphous

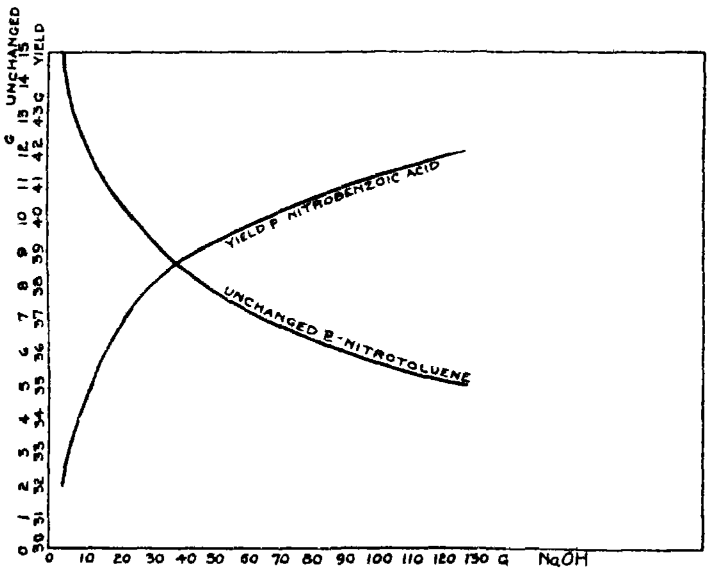

Fig. 5.—*p*-Nitrobenzoic acid produced and *p*-nitrotoluene recovered *vs.* alkali

These results indicated that an increasing percentage concentration of alkali in the solution favors the *p*-nitrotoluene oxidation up to a certain point only, and that the best concentration was that used in Expt. 5. It was employed in most subsequent oxidations.

The influence of dilution was next studied, with the following results:

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[1] Precipitated acid, after filtration, washed by decantation.

TABLE IX.

Influence of Dilution.

Oxidations in the Enamel-Lined Container.

50 g. of *p*-Nitrotoluene and 116 g of Potassium Permanganate Used in Each Experiment.

Expt	Portions $KMnO_4$.	Water Cc	NaOH G	Unchanged *p*-nitrotoluene G	Yield of *p*-nitrobenzoic acid G.	Unchanged + yield G	Character of product.
1 .	15	500	64	14	32	46	Amorphous
2.....	5	1575	64	9	39[1]	48	Amorphous
3.....	3	3150	64	5	43[2]	48	Amorphous
4.....	1	6300	64	6	43[3]	49	Amorphous

Oxidations in the Copper Container.

50 g. of *p*-Nitrotoluene and 128 g. of Potassium Permanganate Used in Each Experiment.

Expt	Portions $KMnO_4$.	Water Cc	NaOH G	Unchanged *p*-nitrotoluene G	Yield of *p*-nitrobenzoic acid G.	Unchanged + yield G	Character of product.
5. .	8	500	0	21 8	22 0	44	....
6.....	8	1575	0	12 4	34 8	47	. ..
7	4	3150	0	9 0	45 0	54	Crystalline (nearly white)

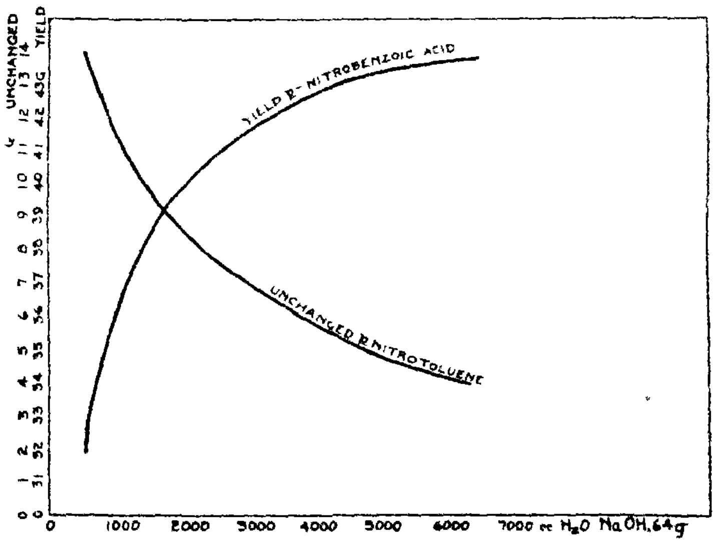

Fig 6—*p*-Nitrobenzoic acid produced and *p*-nitrotoluene recovered *vs.* dilution.

These results show that increasing dilution favors the oxidation both with and without alkali, and that, on the whole, the proportion of water used in Expt. 3 is the best. This was used in subsequent oxidations.

The influence upon the oxidation of employing different amounts of permanganate in excess of the calculated quantity was next investigated. The results are given in the following scheme:

---

[1] Precipitated acid washed by decantation.

[2] Precipitated acid dissolved in alkali, filtered and reprecipitated.

[3] The same amount allowed for inorganic material in the precipitate as was allowed in Expt. 3, *i. e.*, 3 g.

TABLE X.

Influence of Excess of Permanganate

Oxidations in the Enamel Lined Container

50 g. of *p*-Nitrotoluene, 3150 cc. of Water and 64 g of Sodium Hydroxide Used in Each Experiment.

Expt	$KMnO_4$ G	Portions $KNnO_4$	Unchanged *p*-nitrotoluene G	Yield of *p*-nitrobenzoic acid G	Unchanged + yield G	Character of product
1...	116	3	5	43[1]	48	Amorphous
2 ...	122	3	4	40	54	Amorphous
3.. .	128	4	3	52	55	Crystalline
4.. .	141	4	2	52	54	Crystalline
5.... .	155	4	0 4	52	52	Crystalline

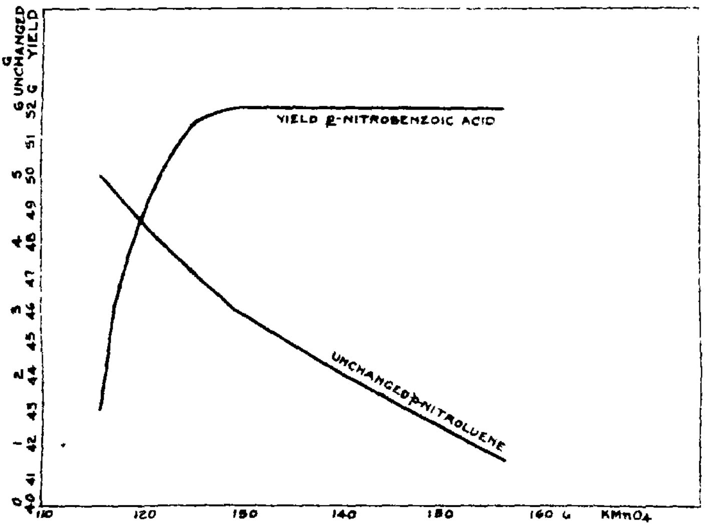

Fig 7.—*p*-Nitrobenzoic acid produced and *p*-nitrotoluene recovered *vs* permanganate in excess of the calculated quantity

The best results were obtained in Expt. 3, in which permanganate 10% in excess of the theoretical amount was used. This excess was subsequently employed, not only in this series of oxidations, but also in the other two series.

A study of the influence of temperature upon the reaction necessitated a slight change in the apparatus, namely, the introduction of a vigorous mechanical stirrer which was used in the oxidations taking place below the boiling temperature of the solution. The results follow:

---

[1] Precipitated acid dissolved in alkali and reprecipitated.

TABLE XI

Influence of Temperature.

Oxidations in the Enamel-Lined Container.

50 g. of *p*-Nitrotoluene, 128 g of Potassium Permanganate in 4 Portions, 3150 cc of Water, and 64 g of Sodium Hydroxide Used in Each Experiment

Expt	Unchanged *p*-nitrotoluene G	Yield of *p*-nitrobenzoic acid G	Unchanged + yield G	Temperature Degrees	Character of product
1	8	46	54	60–65	Very crystalline
2	8	45	53	85	Very crystalline
3	3	52	55	Boiling point	Crystalline

The boiling temperature is thus found to be most favorable to the oxidation. The time of oxidation was greatly increased by a decrease in the temperature. In Expt. 1, it required 2 hours of heating to decolorize 1/4 of the permanganate as compared with approximately 15 minutes in Expt. 3.

The influence of the container upon the oxidation was now studied, both in the neutral and alkaline solutions. The results are given in Table XII.

TABLE XII

Influence of the Container.

50 g of *p*-Nitrotoluene, 128 g of Potassium Permanganate in 4 Portions, 3150 cc. of Water, and 54 g of Sodium Hydroxide Used in Each Experiment.

Expt	Unchanged *p* nitrotoluene G	Yield of *p*-nitrobenzoic acid G	Unchanged + yield G	Container	Character of product
1	4	47	51	Iron	Amorphous
2	6	46	52	Iron	Amorphous
3	4	50	53	Copper	Amorphous but lighter colored
4	3	48	51	Copper	Amorphous but lighter colored
5	3	52	55	Enamel	Crystalline
6	3 8	50	54	Enamel	Crystalline but tinged brown
	No sodium hydroxide used in the following experiments				
7	11	39	50	Iron	Crystalline but tinged brown
8	13	38	50	Iron	Crystalline but tinged pink
9	9	45	54	Copper	Crystalline nearly white
10	10	44	54	Enamel	Crystalline nearly white

These results indicate that oxidations conducted in the iron drum give in all cases both the poorest yield and the poorest quality of product. Those carried out in the copper and enamel containers give approximately the same yields, but the quality of the resulting product is better when the enamel-lined pot is used. In all cases the absence of alkali in the oxidation mixture greatly decreases the yield, but improves the quality of the product. The best appearing product was obtained in Expts. 9 and 10, but it failed to melt any more sharply than the rest.

The best conditions which were attained for the oxidation of *p*-nitrotoluene are those represented in Expt. 5. The amount of material recovered unchanged was at a minimum, and the yield of acid at a maximum.

The product was entirely crystalline, and of a light grayish color. It was obtained in an 85% yield. If the unchanged material is allowed for the yield is raised to 91% of the calculated quantity.

A number of experiments were made studying various isolated influences which may be brought to bear upon the oxidations of *p*-nitrotoluene, which did not fit especially well in any of the above series. The results of these are collected in the following table:

TABLE XIII.

Other Experiments.

Oxidations in the Enamel-Lined Container.

Expt	Portions KMnO	NaOH G	Unchanged *p*-nitrotoluene G	Yield of *p*-nitrobenzoic acid G.	Unchanged + yield G	Character of product.
Using 50 g. of *p*-Nitrotoluene, 128 g. of Potassium Permanganate and 3150 cc. of Water.						
1......	8	64	2	51	53	Crystalline
2......	4	64	3	52	55	Crystalline
3	4	102[1]	11	39	50	Crystalline tinged pink
4.........	4	45[2]	10	38	48	Crystalline tinged pink
5(*a*)......	5	64	6	48	52	Amorphous
Using 50 g. of *p*-Nitrotoluene, 116 g. of Potassium Permanganate and 500 cc. of Water.						
6(*b*).	5	20	25	20	45	Amorphous
7(*b*). ...	15	20	19	25	44	Amorphous
Using 50 g. of *p*-Nitrotoluene, 116 g. of Potassium Permanganate and 3150 cc. of Water.						
8.........	3	128	4	44[3]	48	Amorphous
9(*c*) ...	..	64	4	47[4]	51	Amorphous
Using 100 g. of *p*-Nitrotoluene[4], 256 g. of Potassium Permanganate and 3150 cc. of Water						
10.......	8	64	14	85	99	..

Expts. 1 and 2 indicate the effect upon the oxidation of varying only the number of portions in which the permanganate is added. The smaller number of portions is as advantageous, if not more so, than the larger.

Expts. 3 and 4 show the results of limiting the alkaline strength of the solution to that of $Mg(OH)_2$ and $Ca(OH)_2$, respectively. They also illustrate the influence of the metals, if any. The product obtained under these conditions was of very good quality, but the yield was poor.

Expt. 5 was carried out to show any catalytic effect of pyridine upon the oxidation. The presence of the pyridine only decreased the yield slightly.

In Expt. 9 the permanganate was added gradually, in hot solution, 116 g. of permanganate to 400 cc. of water, to note the effect of increasing to infinity the number of portions in which the oxidizing agent was added. This procedure is troublesome and of no advantage.

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[1] $MgSO_4.7H_2O$. Alkaline strength of $Mg(OH)_2$.

[2] $CaCl_2$, anhydrous. Alkaline strength of $Ca(OH)_2$.

[3] Allowed 4.8% for SiO_2 in the product, according to analysis.

[4] In two 50 g. portions.

(*a*) 25 g. pyridine added.

(*b*) NaOH and water reduced proportionately from Expt. 5, Table VIII.

(*c*) $KMnO_4$ added in solution.

Expt. 10 shows that increasing the concentration of the organic matter in the mixture, while the concentration of alkali in the solution remains constant, decreases the yield obtained.

To determine whether or not *p*-nitrobenzoic acid was oxidized itself by alkaline permanganate, the following experiment was tried. Nine g. of *p*-nitrobenzoic acid, 985 cc. of water, 3 g. of sodium hydroxide, and 21 g. of permanganate (added in 5 separate portions) were boiled together under a reflux condenser. Each portion required about $^3/_4$ hour to become decolorized. When the solution had become colorless, the mixture was filtered and acidified, and there was recovered 6 g. of the acid. Three g. had, therefore, been burned up, which would theoretically reduce 24 g. of permanganate if converted entirely into carbon dioxide and water.

Summary.

A comparative study of experimental conditions, which have an influence on the oxidation of the isomeric nitrotoluenes by means of potassium permanganate in alkaline solution, have led to the following results:

(1) A gradually increasing concentration of alkali in the oxidizing mixture favors the oxidation of *o*- and *p*-nitrotoluene, up to a certain point, while the oxidation of the *m*-compound takes place best in an essentially neutral medium.

(2) An increasing dilution of the solution favors the oxidation of all the nitrotoluenes

(3) *p*-Nitrotoluene is oxidized most readily, the *o*-compound next, and the *m*-derivative least.

In conclusion the writer desires to express his thanks for the constant and friendly interest of Professor Treat B. Johnson, under whose direction this work has been carried out.

NEW HAVEN CONN

[CONTRIBUTION FROM THE LABORATORIES OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH.]

AROMATIC ARSENIC COMPOUNDS. I.

A PLAN OF PROCEDURE FOR THE SYNTHESIS OF ARSENICALS FOR CHEMOTHERAPEUTIC RESEARCH.

BY WALTER A. JACOBS AND MICHAEL HEIDELBERGER.

Received July 2 1919

In the following communications and in those which will appear later, we shall describe certain groups of aromatic arsenic compounds which have been the subject of our studies for several years. In collaboration with Drs. Wade H. Brown and Louise Pearce, who have had charge of the biological phases of the work, we have prepared these substances for the treatment of experimental trypanosome and spirochaete infections.

Although the fundamental types of aromatic arsenic chemistry had been amply studied by Michaelis, the methods at his disposal were such as to limit considerably the development of the field opened up by his researches. The proof by Ehrlich and Bertheim[1] that "atoxyl," obtained by the arsenation of aniline,[2] is the sodium salt of *p*-aminophenylarsonic acid at once led to a great expansion in the study of aromatic arsenic compounds. Ehrlich and those associated with him developed the synthetic possibilities very fully and added greatly to our knowledge in this field. The substances described in their published accounts were mainly those containing one or more of the usual substituents such as amino, hydroxyl, carboxyl, halogen, nitro and the like on the same aromatic nucleus as either trivalent or pentavalent arsenic.

The great practical achievements of this work were the synthesis of diamino-dihydroxy-arsenobenzene (salvarsan base) and the discovery of its great value in the treatment of syphilis and other related diseases. Later synthetic attempts to improve upon this drug were mainly conducted along similar lines, involving the synthesis of substances analogous to salvarsan, of derivatives of the latter and of various metallic coördination compounds of these substances. In the majority of instances the studies have involved compounds in which the chemical variations have been confined to the aromatic nucleus containing the arsenic and it can be assumed that such material has been the subject of fairly exhaustive study.

It seemed wise, therefore, to look in other directions for opportunities for the further synthetic development of arsenic compounds rather than to attempt an extension of the already thoroughly studied groups of substances. However, in the formulation of any comprehensive and systematic developmental policy, it was necessary to keep in mind the biological aim of the work, and in planning our synthetic procedure we have accordingly given special consideration to certain desiderata which we believed essential in this connection. Since these requirements have influenced the character of the substances to be described in the following articles, we feel that a preliminary discussion of these considerations will be appropriate here.

In the first place, work in chemotherapy, to be logical, must be based on the assumption that there is a relationship between chemical constitution and biological action. The substances to be chosen should therefore be of such a character as to permit interpretation of the biological action as a function of chemical structure, in order that the data obtained may be used in the further prosecution of the work. This can be consistently carried out only when the compounds studied are sufficiently alike in general structure to reduce to a minimum the number of chemical features which must be considered in contrasting the biological properties of compounds in order to arrive at the chemical cause of the observed variations in action. The conditions for such homogeneity of material can best be realized by confining the studies to a group of closely related substances which may be regarded as derivatives of some parent compound. The various chemical modifications in the series of drugs would then be chiefly in the nature of the addition to the molecule of groups or side chains, readjustments in their relative positions or alterations confined to such groups or side chains.

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[1] *Ber.*, 40, 3292 (1907).

[2] Béchamp, *Bull. soc. chim.*, 5, 518 (1863).

In the selection of the types of substances due consideration should be given to the technical character of the work involved in their preparation. As the efficient prosecution of work in chemotherapy can be accomplished only by the intimate and parallel coöperation of both the biological and the chemical sides, preparative difficulties can not be allowed to consume a disproportionate amount of time and effort. It is desirable, therefore, that the types chosen represent readily accessible groups of substances. These types also should be of such a character as to permit of ready chemical modification by the addition of new groups or side chains which may in turn be altered at will as regards number, character, or position. It is important when a certain chemical modification is suggested as particularly desirable from a study of the biological results, that the modification be reasonably easy to execute. Otherwise, as has only too often occurred, the work will be brought to a standstill because of the difficulty of developing further a chemical lead which has been presented.

The realization of these requirements can be made easier if the substances chosen are prepared by reactions of a simple type. For this purpose as starting material there is chosen a readily obtainable substance which contains on the one hand the therapeutic element or radical, and on the other hand some reactive group such as, for example, the amino group. Each new compound would then be produced by the reaction of this starting material with a second class of substances, each of which possesses the same suitably reactive group as, for instance, aliphatically bound halogen. The production of the final compounds would in each case depend mainly on the accessibility of this second group of substances. It may not be irrelevant to point out that accessibility is not only an important aid to scientific orientation, but also determines the cost of any remedy which might be developed. Finally, for practical reasons, substances which can be dissolved in water are most desirable.

From a purely chemical standpoint, in applying these requirements to the preparation of arsenic compounds for biological study, it was obvious from the first that pentavalent arsenic compounds would offer the best material for initial explorations. The trivalent arsenic derivatives as a class do not meet with the technical requirements as above set forth, whereas the more available, more easily handled, and more stable pentavalent compounds promised to afford wider opportunities for synthetic work. These substances, possessing the arsenic as the salt-forming arsonic acid residue, at once solved the problem of solubility. For biological work, arseno compounds, on the other hand, are restricted to those which possess other salt-forming groups and are therefore far more limited than the pentavalent compounds. We are inclined to regard reduction to the arseno form more as a chemical modification which could ultimately be attempted where the presence of a non-arsenical solubilizing group might make this desirable.

Arsanilic acid, the most accessible of the aromatic arsenic compounds, was naturally chosen as the fundamental substance. This compound contains not only the therapeutic element arsenic, in a salt-forming combination, but also carries a very reactive amino group. As Ehrlich and Bertheim have amply shown, it can be subjected to all the reactions which characterize primary aromatic amino compounds. It therefore afforded the logical and ideal starting material for the synthetic treatment outlined above. By choosing the proper reaction it was possible to make use of this amino group in such a way as to form a side chain which served the function of a connecting link between the benzene nucleus containing the arsenic and another group in which the chemical alterations were made. Moreover, in particular cases in which an optimal effect had been achieved with a substance derived from arsanilic acid, the opportunity always remained for studying the further effect of changes in position or of the addition of new groups in the nucleus containing the arsenic, by making the analogous substance derived from the isomers, homologs or other substitution products of arsanilic acid.

p-Hydroxy-phenylarsonic acid, another easily available aromatic arsenic compound, offered similar possibilities by virtue of the hydroxyl group, although this is more limited in reactivity than the amino group.

The following types which were developed in the present work will present this plan of procedure in more concrete form:

I. Diazoamino Compounds, $A-N=N-NRR'$, in which A is the arylarsonic acid radical and R and R′ hydrogen, alkyl, aryl or substituted aryl groups.

As Ehrlich and Bertheim have shown, arsanilic acid may be readily and quantitatively diazotized and the diazo compound coupled with appropriate couplers to form azo dyes. We have likewise found that the diazo compound couples in a normal manner with suitable secondary aliphatic amines and primary and secondary aromatic amines to form diazoamino compounds. The same result could also be obtained in the case of the primary aromatic amines by first diazotizing these and coupling the resulting diazonium salts with arsanilic acid. The compounds obtained from the aromatic amines suited our purpose best.

II. Azo Dyes, A — N = N — R, in which A is the arylarsonic acid radical and R is the aromatic coupler.

III. *N*-Substituted Amides of *N*-Phenylglycine-*p*-arsonic Acid, A—$NHCH_2CONRR'$ in which R and R′ are hydrogen, alkyl, aryl or substituted aryl groups.

As a primary amino compound, arsanilic acid should react with alkyl halides to form *N*-alkyl derivatives. In the particular direction in which we chose to employ this reaction, its practicability had already been suggested by the preparation of the single substance, phenylglycine-*p*-arsonic acid, from arsanilic acid and chloroacetic acid.[1] We have demonstrated, as was to be expected, that this reaction could be extended to chloroacetyl compounds in general. Our attention was centered mainly upon the development of a series of compounds by the use of the chloroacetyl derivatives of primary and secondary aliphatic or aromatic amines.

IV. β-Substituted Ureides of *N*-Phenylglycine-*p*-arsonic Acid, A—$NHCH_2CONHCONHR$.—This type of substance is closely related to the previous one and was in like manner easily prepared from arsanilic acid and the chloroacetyl uramino compounds, $ClCH_2CONHCONHR$ in which R may be hydrogen, or an alkyl, aryl, or substituted aryl group.

V. Substituted *N*-Phenylglycyl Derivatives of Arsanilic Acid, A—$NHCOCH_2NHR$.—Type III naturally suggests a parallel series of compounds in which the side-chain joining the two benzene nuclei is reversed. These substances were prepared with remarkable readiness from chloroacetylarsanilic acid and primary or secondary amino compounds.

VI. Substituted *o*-Phenyl Glycollyl Derivatives of Arsanilic Acid.—When the amine in the preceding series was replaced by a phenol in alkaline solution, chloroacetylarsanilic acid was found to react smoothly in the proper sense, yielding substituted *o*-phenyl glycollyl derivatives of arsanilic acid, of the following general formula: A—$NHCOCH_2OR$.

VII. Substituted Amides of *o*-Phenyl Glycollic Acid *p*-Arsonic Acid, A —*o*-CH_2CONHR.

By a reaction identical with that given in Type VI, only starting with *p*-hydroxyphenyl arsonic acid and chloroacetylamino compounds, an analogous type of substances was prepared, differing from Type VI in that the side chain connecting the two nuclei is reversed.

Still other types were similarly studied.

Since the development of Type III has led to the most important results in the present work we shall confine the discussion to this group of substances. In this type the fundamental member of the series is *N*-phenylglycinamide-*p*-arsonic acid,

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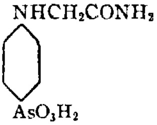
[1] Ger. pat. 204,664.



This substance was prepared by the simple reaction of chloroacetamide on the sodium salt of arsanilic acid. By replacing the chloroacetamide by chloroacetylalkyl amines a limited series of compounds was prepared, which naturally preceded those of the aromatic series. The broadest scope for synthetic work, of course, was furnished by the aromatic series, compounds of this type being obtained from substituted chloroacetylarylamines and arsanilic acid.

This sub-group possesses two aromatic nuclei, an arsenical nucleus and a non-arsenical nucleus. It is apparent that by the choice of the proper chloroacetylarylamine any desired chemical groupings on the non-arsenical nucleus could be obtained. These could be made to vary at will as regards the character, number, and position of the substituting groups. And as the resulting substances were all obtained by the same reaction the technique of their preparation was easily standardized. The availability of any substance of this series was therefore determined only by the accessibility of the aromatic amine from which the chloroacetyl compound was prepared. As the alterations in the chemical groupings were first confined to the non-arsenical nucleus, each individual substance could be considered to be derived from the same parent type. Insofar as the biological action can be interpreted as a function of constitution, such a series therefore offered the opportunity of determining the biological value of each group, or of the position which it occupied in the nucleus. The correlation of the chemical and biological facts obtained with such homogeneous material offered a good opportunity for concluding in what direction new alterations within the same type should be attempted. And as the type was composed of available substances such dictates were generally possible to follow.

It was thus the purpose at first to confine the chemical alterations to the non-arsenical nucleus. But ultimately by employing a homolog, isomer, or other substitution product of arsanilic acid, modifications on the arsenical nucleus were attempted. Finally the side chain—$NHCH_2CONH$—which serves as the link between the two nuclei was also made the place for chemical alterations without destroying the relationship of the resulting compounds to the original type. This group could be changed to the chain—$NHCHRCONH$—in which R could be alkyl or aryl. Variations of this nature were generally made, not on a finished substance of Type III, but on an intermediate product; for example, if R is phenyl, such compounds were prepared by reacting arsanilic acid with phenylchloroacetyl amino compounds.

By the above treatment of the subject we have attempted to realize the conditions postulated at the start as essential in a logical plan for the synthesis of new arsenicals for biological study. It is our belief that a similar treatment of other leads, where chemically possible, will prove of service in chemotherapeutic investigations.

New York, N. Y.

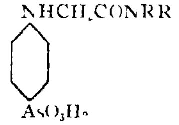
[Contribution from the Laboratories of the Rockefeller Institute for Medical Research.]

AROMATIC ARSENIC COMPOUNDS. II. THE AMIDES AND ALKYL AMIDES OF *N*-ARYLGLYCINE ARSONIC ACIDS.

By Walter A. Jacobs and Michael Heidelberger.

Received July 2, 1919.

As in the case of other aromatic amino compounds, sodium *p*-aminophenylarsonate (sodium arsanilate) has been found to react with chloroacetic acid to form phenylglycine-*p*-arsonic acid.[1] In the present investigations we have found that the amide and alkyl amides of chloroacetic acid react in similar manner to form the amide and alkyl amides of phenylglycine-*p*-arsonic acid, with the following general formula



in which R and R' may be hydrogen, alkyl, benzyl or substituted benzyl radicals. Although arsanilic acid itself may be employed in this reaction instead of the sodium salt, the reactivity of the amino group is suppressed by the negative arsonic acid radical so that the reaction proceeds very slowly, and satisfactory yields are only obtained when an extra molecule of the amino acid is employed, since the hydrochloric acid produced during the condensation renders a portion of the base inactive. On the other hand sodium arsanilate exhibits the full reactivity of the amino group and the sodium ion present neutralizes the hydrochloric acid as it is formed.

Chloroacetamide and the simpler chloroacetyl alkylamines condensed readily with sodium arsanilate in boiling aqueous solution, and although the reaction in no instance proceeded quantitatively, owing to the occurrence of side reactions, 1/2 to 2 hours' boiling sufficed for obtaining optimum yields. In the case of the chloroacetylbenzyl amines, 50% alcohol was found to be the most serviceable medium owing to the sparing solubility of these compounds in water. Moreover, the reactivity of the chlorine atom in these substances proved to be so much less than that of the simpler alkyl derivatives that the addition of sodium iodide was found necessary, greatly facilitating the condensation owing to the intermediate formation of the iodoacetyl derivatives.

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[1] Ger pat. 204,664.

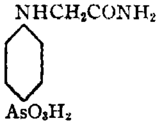
The first member of the series, *N*-phenylglycineamide-*p*-arsonic acid, was also prepared by the action of concentrated ammonia on the methyl ester of phenylglycine-*p*-arsonic acid. This method could unquestionably be employed for the preparation of the simpler homologous compounds, in which case it would necessitate the recovery of the excess of the expensive amines.

The present studies on *p*-arsanilic acid were extended to include analogous substances starting with *o*- and *m*-arsanilic acids and the homologous aminoaryl arsonic acids.

All of the glycineamide arsonic acids are colorless, crystalline substances which are as a rule but sparingly soluble in the usual neutral solvents and possess high melting or decomposition points, the latter depending greatly upon the rate of heating. As arsonic acids they dissolve in alkalies and alkaline carbonates to form neutral salts, but are completely displaced from these by so weak an acid as acetic acid. Because of the imino group they also possess basic properties and form nitroso derivatives. The basicity appears to be more feeble than that of arsanilic acid itself, since these substances dissolve or form stable hydrochlorides only in strong hydrochloric acid, the salts being easily hydrolyzed by water. On boiling with an excess of alkali or with mineral acids the amide linking is hydrolyzed with the formation of the glycine arsonic acid and the amine.

In the experimental part of this and subsequent papers a description of the sodium salts will be frequently encountered. In many cases these afforded a means for purifying such crude reaction products as could not be directly recrystallized, but the majority were prepared in order to furnish substances in a readily soluble form convenient for biological testing.

Since the results obtained with the first member of the group, *N*-phenylglycinamide-*p*-arsonic acid,



in the treatment of experimental trypanosome and spirochaete infections have been of so promising a character and because of its low toxicity, this substance has been made the subject of extensive study.[1] The biological results are being published elsewhere by our colleagues, Drs. Brown and Pearce. Because of the importance of this compound we are presenting it and the other derivatives obtained from *p*-aminophenyl arsonic acid first, the derivatives of *o*- and *m*-aminophenyl arsonic acids following these.

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[1] It may be appropriate to mention here that this substance and related com-

EXPERIMENTAL.

(A) Derivatives of *p*-Aminophenyl Arsonic Acid.

***N*-(Phenyl-4-arsonic acid)glycineamide (*N*-Phenyl-glycineamide-*p*-arsonic acid).**—Of the two methods used for the preparation of this substance that described first is perhaps to be preferred.

434 g. of arsanilic acid[1] were dissolved in 2 liters of *N* sodium hydroxide solution. After adding 375 g. of chloroacetamide[2] the mixture was boiled under a reflux condenser for 45 minutes, the clear solution setting to a solid mass of the crude product on cooling. 75 cc. of conc. hydrochloric acid were added to the cold mixture to hold any unchanged arsanilic acid in solution and the substance was then filtered off and carefully washed with cold water. For purification it was suspended in sufficient water to form a thin paste and carefully treated, with stirring, with 25% sodium hydroxide solution until the acid was completely dissolved. The filtered solution was then treated with an excess of acetic acid, whereupon the substance separated as minute, lustrous plates. After filtering, washing thoroughly, and drying, the yield was 300 g. The use of the above amount of chloroacetamide, though twice that theoretically required, was found advisable in order to obtain a good yield. The *acid* is very sparingly soluble in cold water, but dissolves readily on heating. It separates from the hot, aqueous solution in aggregates of

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pounds, described in the present and following papers of the series, are covered by U. S. Patents, Nos. 1,280,119–27. Patents have also been applied for in foreign countries.

All discoveries made at the Rockefeller Institute are made freely available to the public, in accordance with the philanthropic purposes of the institution. In order to insure purity of product and protection against exploitation, it has been deemed necessary in certain instances to protect the discoveries by patents It is the purpose of the Institute to permit any drugs which may prove of practical therapeutic value to be manufactured under license by suitable chemical firms and under conditions of production which will insure the biological qualities of the drugs and their marketing at reasonable prices. Other than through the issuance of license, the Rockefeller Institute does not participate in any way in the commercial preparation or sale of the manufactured chemicals; and it receives no royalties or other pecuniary benefits from the licenses it issues.

[1] The first portions of this and several other arylarsonic acids were kindly furnished before the war by L Cassella and Co. and the Farbwerke Höchst Later, when larger amounts of arsanilic acid were required it was prepared by us by heating aniline and arsenic acid, although we soon adopted a modification of this general method kindly placed at our disposal by Dr G. W. Raiziss, of the Dermatological Research Laboratories of Philadelphia.

[2] *J. Biol. Chem.*, **21**, 145 (1915).

long, thin plates. It is insoluble in methyl alcohol, acetone or chloroform, and sparingly in hot methyl or ethyl alcohol, but dissolves in boiling acetic acid. It is sparingly soluble in dil. hydrochloric acid but dissolves readily in the strong acid, its behavior showing it to be a weaker base than arsanilic acid. On boiling its solution in sodium hydroxide ammonia is evolved. When rapidly heated in an open capillary tube it darkens and softens at 280°, but does not melt.

Subs., 0.1405 g.: 12.35 cc. N (22.0°, 761 mm). Subs. 0.3205: $Mg_2As_2O_7$ 0.1832
Calc. for $C_8H_{11}O_4N_2As$: N, 10.22; As, 27.33. Found: N, 10.18; As, 27.59.

Salts.—The pure acid is suspended in enough water to form a thick paste and carefully treated with 25% sodium hydroxide solution until completely dissolved and the solution reacts neutral to litmus. Two volumes of alcohol are then added, the pure *sodium salt* quickly separating as thin, nacreous plates. After filtering and washing with 85% alcohol it is air dried and then contains $^1/_2$ molecule of water of crystallization. The sodium salt is extremely soluble in cold water, the solution reacting neutral to litmus.

Subs., air-dry: 0.3921. Loss, 0.0117 *in vacuo* over H_2SO_4 at 100°
Calc. for $C_8H_{10}O_4N_2AsNa.0.5H_2O$. H_2O, 2.95 Found. 2.98
Subs., anhydrous, 0.1503: 12.45 cc N (25.0°, 762 mm.) Subs. 0.2300 Mg_2As_2O, 0.1195.
Calc. for $C_8H_{10}O_4N_2AsNa$ N, 9.46, As, 25.32. Found N, 9.52; As, 25.08

The *potassium* and *ammonium salts* were prepared in the same way as the sodium salt and form thin, glistening, hexagonal, microscopic platelets. On adding a calcium chloride solution to a solution of the sodium salt the *calcium salt* gradually separates as microscopic, wedge-shaped prisms, containing no water of crystallization. Magnesia mixture causes no precipitate in the cold, but on warming the *magnesium salt* separates as a microcrystalline powder. Heavy metal salts give immediate precipitates, the *silver salt* forming aggregates of thin, microscopic needles.

N-Phenyl-glycinamide-*p*-arsonic acid was also prepared as follows from *N*-phenyl-glycine methyl ester *p*-arsonic acid by the action of ammonia.

***N*-(Phenyl-4-arsonic acid) glycine methyl ester,** *p*-$H_2O_3AsC_6H_4NHCH_2$-$COOCH_3$.—40 g. of *N*-phenyl-glycine-*p*-arsonic acid[1] were treated with 120 g. of dry methyl alcohol and 12 g. of conc. sulfuric acid. The mixture was boiled under a reflux condenser for two hours. The ester separated on cooling and scratching, the precipitation being completed by the addition of water. The filtered, washed, and dried product weighed 38 g. It can be recrystallized from hot water or hot 95% alcohol, separating from the former as microscopic needles and thin plates. It is very sparingly soluble in cold water, cold alcohol, or boiling acetone, and is fairly easily soluble in methyl alcohol, especially on warming. When rapidly heated it softens and darkens above 200° and decomposes at about 285°.

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[1] Ger. pat. 204,664.

Subs. 0.1560 7.0 cc N (21.0°, 747 mm.). Subs. 0.3135. $Mg_2As_2O_7$, 0.1665.
Calc. for $C_9H_{12}O_6NAs$: N, 4.84; As, 25.94 Found. N, 5.12; As, 25.63.

The ester was converted into the amide as follows: 10 g. of the ester were slowly added, with stirring, to 30 cc. of well chilled, conc. ammonia. At first a thick paste of the ammonium salt of the ester was formed, but on allowing the mixture to rise to room temperature the reaction proceeded with formation of a clear solution. After 24 hours the excess of ammonia was removed, preferably *in vacuo*. On diluting with water, filtering, and acidifying with acetic acid, phenyl-glycineamide-*p*-arsonic acid separated in characteristic form. This was purified as described above and was identical in every way with the product obtained by the direct method. The yield was 80% of the theoretical amount.

Subs. 0.1297: 11.5 cc N (19.5°, 742 mm.)
Calc. for $C_8H_{11}O_4N_2As$: N, 10.22. Found. 10.11.

N-(**Phenyl-4-arsonic acid)glycine ethyl ester,** *p*-$H_2O_3AsC_6H_4NH$-$CH_2CO_2C_2H_5$.—Recrystallized from 50% alcohol the ethyl ester forms flat, delicate needles which melt and decompose at about 270° with preliminary darkening and softening. It is very difficultly soluble in cold water, rather more soluble in cold alcohol, but dissolves quite readily in either solvent on boiling.

Subs., 0.1944: (Kjeldahl) 9.3 cc 0.0714 *N* HCl Subs., 0.3287 $Mg_2As_2O_7$, 0.1703.
Calc. for $C_{10}H_{14}O_6NAs$: N, 4.62; As, 24.72 Found N, 4.78; As, 25.01

N-(**Phenyl-4-arsonic acid)nitroso-glycineamide,** *p*-$H_2O_3AsC_6H_4N$-(NO)CH_2CONH_2.—3 g. of the air-dry sodium salt were dissolved in 10 cc. of water and 2 cc. of 5 *N* sodium nitrite solution (1 mol.) added. On addition of 5 cc. of 1 : 1 hydrochloric acid (a little over 2 mols.) the rapid separation of characteristic crystals of unchanged phenyl-(4-arsonic acid)-glycineamide occurred, but on gentle warming the crystals suddenly changed to delicate needles and the mixture set to a solid cake. After diluting somewhat with water the cooled mixture was filtered, and the nitroso compound recrystallized from water, in which it is readily soluble at the boiling point and only sparingly in the cold. It forms rosets and sheaves of silky needles which intumesce at 182–3°, with preliminary yellowing, when rapidly heated to 180°, then slowly. The acid is difficultly soluble in cold methyl or ethyl alcohol, more easily on boiling, and dissolves only sparingly in cold acetic acid although quite readily in the boiling acid. It turns yellow under sulfuric acid, dissolving to an almost colorless solution giving a brown-red Liebermann test.

Subs., 0.1116: 13.6 cc. N (25.5°, 758 mm.). Subs., 0.2763: $Mg_2As_2O_7$, 0.1412.
Calc. for $C_8H_{10}O_5N_3As$. N, 13.87; As, 24.72. Found: N, 13.90; As, 24.65.

***N*-(Phenyl-4-arsonic acid)glycine methyl amide,** p-$H_2O_3AsC_6H_4NHCH_2CONHCH_3$.—44 g. of arsanilic acid dissolved in 200 cc. of *N* sodium hydroxide solution,[1] and 25 g. of chloroacetyl-methylamine[2] were boiled under a reflux condenser for one hour. The acid separated from the solution on cooling and scratching and was purified by dissolving in just enough dilute sodium hydroxide solution and reprecipitating with acetic acid. The substance separated as a thick mass of thin, microscopic plates. The yield was 31 g. The acid is fairly easily soluble in hot water, from which it separates as aggregates of curved spears. It is difficultly soluble in methyl alcohol and may be recrystallized from hot 50% alcohol. It darkens and softens above 240° and decomposes after a few moments at 285°.

Subs., 0.3269 (Kjeldahl) 22.4 cc 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1755.
Calc. for $C_9H_{13}O_4N_2As$ N, 9.73; As, 26.00. Found: N, 9.60; As, 25.91.

***N*-(Phenyl-4-arsonic acid)glycine ethyl amide,** p-$H_2O_3AsC_6H_4$-*$NHCH_2CONHC_2H_5$.—44 g. of arsanilic acid and 30 g. of chloroacetyl*-ethylamine,[3] were condensed as in previous examples. For purification the resulting ethylamide was dissolved in a small volume of hot water, from which it separated on cooling as a thick crust of platelets. The yield was 30 g. The acid is sparingly soluble in cold water or alcohol, but dissolves readily on warming. It is soluble in methyl alcohol, particularly on warming. The substance darkens above 250° and decomposes at 278–80°. Attempts to make a pure sodium salt were unsuccessful owing to its great solubility in water or dilute alcohol.

Subs., 0.1441: 11.6 cc. N (21.0°, 762 mm.). Subs., 0.3707. $Mg_2As_2O_7$, 0.1923.
Calc. for $C_{10}H_{15}O_4N_2As$. N, 9.27; As, 24.81. Found. N, 9.37, As, 25.04.

***N*-(Phenyl-4-arsonic acid)glycine *n*-propyl amide,** p-$H_2O_3AsC_6H_4NHCH_2CONHCH_2CH_2CH_3$.—4.4 g. of arsanilic acid and 3 g. of chloroacetyl-propylamine[2] yielded after two hours an oil which crystallized when rubbed. This was purified by dissolving in hot, dil. ammonia and acidifying with acetic acid. It separated slowly on cooling as flat needles or plates and wedge-shaped prisms. The yield was 3.5 g. The substance is sparingly soluble in boiling water, but readily so in boiling 50% alcohol, from which it separates on cooling as sheaves of microscopic needles. It does not melt below 280°.

Subs., 0.1491: 11.6 cc. N (22.5°, 758 mm.). Subs., 0.3188: $Mg_2As_2O_7$, 0.1549.
Calc. for $C_{11}H_{17}O_4N_2As$: N, 8.86; As, 23.70. Found: N, 8.96; As, 23.45.

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[1] Hereafter unless otherwise stated arsanilic acid was always dissolved in the equivalent amount of *N* sodium hydroxide solution and likewise equivalent quantities of the halide were employed for the reaction.

[2] This Journal, 41, 472 (1919).

[3] *J. Biol. Chem.*, 21, 149 (1915).

***N*-(Phenyl-4-arsonic acid)glycine dimethyl amide,** *p*-$H_2O_3AsC_6H_4$-$NHCH_2CON(CH_3)_2$.—After ½ hour's boiling the reaction product from 3 g. of chloroacetyl-dimethylamine[1] suddenly separated as a mass of thin, microscopic needles, often occurring in characteristic sheaves. After cooling the mixture was acidified with hydrochloric acid, filtered and the substance washed with water. It was recrystallized from 50% alcohol, requiring a large volume and separating in the same characteristic form. The yield was 3 g. The substance is very sparingly soluble in the neutral solvents, and when rapidly heated, decomposes at about 241–2°.

Subs., 0.1392: 11.1 cc. N (22.0°, 762 mm). Subs., 0 3440: $Mg_2As_2O_7$, 0.1747.
Calc. for $C_{10}H_{15}O_4N_2As$: N, 9.27; As, 24.81. Found· N, 9.25; As, 24.50.

Sodium Salt.—A neutral solution of the acid in dil. sodium hydroxide, on treating with two volumes of alcohol, yielded the salt as elongated plates, which after washing with 50% alcohol and air drying contained 4 molecules of water of crystallization and dissolved easily in water.

Subs , air-dry, 0.4277 loss, 0.0782 *in vacuo* at 80° over H_2SO_4.
Calc. for $C_{10}H_{14}O_4N_2AsNa.4H_2O$· H_2O, 18.19. Found· 18.28.
Subs., anhydrous, 0.2985· (Kjeldahl) 18.35 cc. 0.1 *N* HCl.
Calc. for $C_{10}H_{14}O_4N_2AsNa$: N, 8.65. Found. 8.61.

***N*-(Phenyl-4-arsonic acid)glycine diethyl amide,** *p*-$H_2O_3AsC_6H_4NH$-$CH_2CON(C_2H_5)_2$.—After one hour 4 g. of chloroacetyl-diethylamine[2] yielded an oil on cooling which soon crystallized. This was purified by dissolving in just enough dil. sodium hydroxide solution and reprecipitating with acetic acid, forming microscopic aggregates of short needles. The yield was 4 g. When rapidly heated it sinters and darkens above 195° and melts at 199–201° with gas evolution. It is difficultly soluble in boiling water but dissolves in boiling methyl alcohol or 50% alcohol.

Subs , 0 3184 (Kjeldahl) 18 95 cc 0.1 *N* HCl, $Mg_2As_2O_7$, 0.1497.
Calc. for $C_{12}H_{19}O_4N_2As$. N, 8.49; As, 22.69. Found· N, 8.34; As, 22.68.

***N*-(Phenyl-4-arsonic acid)glycine piperidide,** *p*-$H_2O_3AsC_6H_4NHCH_2$-$CONC_5H_{10}$.—From 4 g. of chloroacetyl-piperidine[3] there resulted after two hours' boiling a viscous oil which readily crystallized. This was filtered off, washed with water, and finally with 50% alcohol to remove traces of an adhering oil. The residue was then recrystallized from hot 50% alcohol, separating in characteristic sheaves of thin microscopic needles which soften and darken above 200° and decompose at 218–21°. The yield was 3 g. The acid is soluble in hot methyl alcohol and hot 50% alcohol, but very sparingly soluble in hot water.

Subs., 0.1433: 9.95 cc. N (22.5°, 762 mm.). Subs., 0.3055: $Mg_2As_2O_7$, 0.1400.
Calc. for $C_{13}H_{19}O_4N_2As$ N, 8.19; As, 21.90 Found: N, 8.05; As, 22.12.

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[1] *J. Biol. Chem.*, **21**, 148 (1915).

[2] *Ibid.*, **21**, 149 (1915).

[3] THIS JOURNAL, **41**, 473 (1919).

***N*-(Phenyl-4-arsonic acid)glycine benzyl amide,** *p*-$H_2O_3AsC_6H_4NH$-$CH_2CONHCH_2C_6H_5$.—Since chloroacetyl-benzylamine[1] and its derivatives reacted relatively slowly and incompletely with arsanilic acid, it was found that the reaction could be greatly facilitated by the addition of equivalent amounts of sodium iodide to the reaction mixture, owing to the intermediate formation of the more reactive iodoacetyl derivatives, the medium used being 50% alcohol.

4.4 g. of arsanilic acid dissolved in 20 cc. of *N* sodium hydroxide solution, 3.7 g. of chloroacetyl-benzylamine, 4 g. of sodium iodide, and 20 cc. of alcohol were heated under a reflux condenser for 4 hours. On cooling the clear solution thickened to a paste of crystals. The collected reaction product was purified by dissolving in sufficient dil. sodium hydroxide solution and acidifying with acetic acid and again recrystallized from hot 85% alcohol, from which it slowly separated as microscopic needles. The yield was 3 g. The acid is soluble in boiling 50% or 85% alcohol and in boiling methyl alcohol, but very sparingly in boiling water. It decomposes at 282–4°.

Subs., 0 2952· (Kjeldahl) 16.25 cc. 0 1 *N* HCl; Mg_2As_2O , 0 1250
Calc. for $C_{15}H_{17}O_4N_2As$· N, 7.70; As, 20.58. Found N, 7 71, As, 20.43.

***N*-(Phenyl-4-arsonic acid)glycine 3′-carboxamido benzyl amide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHCH_2C_6H_4CONH_2$(*m*-).—In a similar manner 22.5 g. of *m*-carboxamido-chloroacetyl-benzylamine,[2] gave a clear solution which on standing and scratching deposited 27.5 g. of crude product. This was purified by dissolving in the requisite amount of dil. sodium hydroxide solution or ammonia and reacidifying with acetic acid. It separated gradually as thick aggregates of microscopic needles. On continued washing with water it tends to become colloidal. The arsonic acid decomposes at 237–9° with preliminary darkening. It is sparingly soluble in hot water, and boiling acetic acid and practically insoluble in boiling alcohol.

Subs., 0.3431: (Kjeldahl) 25.42 cc. 0.1 *N* HCl, Subs. 0 3693 Mg_2As_2O., 0 1400.
Calc. *for* $C_{16}H_{18}O_5N_3As$ N, *10.32; As, 18,40.* Found N, *10 37; As, 18.29.*

Sodium Salt.—The acid was suspended in a small volume of hot water and 25% sodium hydroxide solution added cautiously until the solution cleared and reacted neutral to litmus. On chilling the sodium salt separated in rosets and sheaves of delicate needles, which were filtered off, washed with ice water, and air-dried. The salt separates with 5 molecules of water of crystallization and is freely soluble in water and salted out from concentrated solutions by sodium acetate.

Subs., air-dry, 0.8918: loss, 0.1520 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{16}H_{17}O_5N_3AsNa.5H_2O$ H_2O, 17.35. Found 17 05.

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[1] *J. Biol. Chem.*, **20**, 686 (1915).

[2] *Ibid.*, **20**, 694 (1915).

Subs., anhydrous, 0.3929: (Kjeldahl) 27.35 cc. 0.1 N HCl.
Calc. for $C_{16}H_{17}O_6N_3AsNa$: N, 9.79. Found: 9.75.

N-(Phenyl-4-arsonic acid)glycine 4′-acetamino benzyl amide, *p*-$H_2O_3AsC_6H_4NHCH_2CONHCH_2C_6H_4NHCOCH_3$(*p*-).—After several hours' boiling the arsonic acid resulting from 4.8 g. of *p*-acetaminochloroacetyl-benzylamine,[1] separated from the hot solution, and after washing with 50% alcohol amounted to 5.5 g. It was purified by reprecipitating its solution in dil. ammonia with acetic acid, separating as flat, microscopic needles. The acid is almost insoluble in the usual solvents except hot 50% alcohol from which it separates on cooling as diamond-shaped plates. It darkens and sinters partly but does not melt below 280°.

Subs., 0.3024 (Kjeldahl) 21.4 cc 0.1 N HCl. Subs., 0.3824: $Mg_2As_2O_7$, 0.1399.
Calc. for $C_{17}H_{20}O_5N_3As$: N, 9.98; As, 17.78. Found. N, 9.91, As, 17.65.

Sodium Salt.—On treatment of the clear, neutral solution of the acid in dil. sodium hydroxide with several volumes of alcohol and scratching, the salt separated as microscopic needles. These were filtered off, washed with 95% alcohol, and air-dried, then containing 4.5 molecules of water of crystallization. The salt is readily soluble in water.

Subs., air-dry, 0.6157. loss, 0.0965 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{17}H_{19}O_5N_3AsNa$ $4.5H_2O$: H_2O, 15.46. Found: 15.67.
Subs., anhydrous, 0.2974: (Kjeldahl) 20.2 cc. 0.1 N HCl; $Mg_2As_2O_7$, 0.1050.
Calc. for $C_{17}H_{19}O_5N_3AsNa$: N, 9.48; As, 16.91. Found: N, 9.52, As, 17.03.

N-(Phenyl-4-arsonic acid)glycine 3′-carboxureidobenzyl amide, *p*-$H_2O_3AsC_6H_4NHCH_2CONHCH_2C_6H_4CONHCONH_2$(*m*-).—During the condensation with sodium arsanilate the almost insoluble *m*-(ω-chloroacetylaminomethyl)benzoyl-urea[2] gradually changed its appearance owing to the deposition of the reaction product. After 4 hours the mixture was diluted with water, made alkaline with ammonia, warmed, and filtered. On acidification with acetic acid the filtrate yielded a colorless, crystalline powder. This was filtered off, redissolved in hot dil. ammonia, boiled with bone black, and the hot filtrate treated with acetic acid. The arsonic acid separated as glistening, microscopic aggregates of delicate needles which decompose at 239–40° when rapidly heated and are practically insoluble in the usual neutral solvents. The yield was unusually poor.

Subs., 0.1119: 12.4 cc. N (27.0°, 754 mm.). Subs., 0.3052: $Mg_2As_2O_7$, 0.1042.
Calc. for $C_{17}H_{19}O_6N_4As$. N, 12.45; As, 16.65. Found: N, 12.52; As, 16.48.

N-(Phenyl-4-arsonic acid) 4′-uramino benzyl amide, *p*-$H_2O_3AsC_6H_4NHCH_2CONHCH_2C_6H_4NHCONH_2$(*p*-).—As the reaction mixture obtained from *p*-uramino-chloroacetyl-benzylamine[3] remained clear on cooling, most of the alcohol was boiled off and water added. On cooling an oil separated which gradually crystallized. The filtered product was dissolved in dil. sodium hydroxide solution and exactly neutralized with acetic acid. After standing in the refrigerator for 24 hours the solution was filtered from a slight precipitate, but as the sodium salt could not be obtained crystalline by any of the usual methods, the solution was treated with an excess of acetic acid, again causing the separation of the arsonic acid as an oil which gradually crystallized on standing. The purification process was repeated, resulting in considerable loss, the final yield being rather poor. For analysis the substance was dried *in vacuo* at 100°.

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[1] Einhorn and Mauermayer, *Ann.*, **343**, 299 (1905).

[2] THIS JOURNAL, **39**, 2432 (1917).

[3] *Ibid.*, **39**, 2442 (1917).

Subs., 0.3747 (Kjeldahl) 34.8 cc. 0.1 *N* HCl, $Mg_2As_2O_7$, 0.1360.

Calc. for $C_{16}H_{19}O_5N_4As$: N, 13.27, As, 17.76. Found: N, 13.01, As, 17.52.

***N*-(Phenyl-4-arsonic acid)glycine 3'-methyl-4'-acetamino benzyl amide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHCH_2C_6H_3(CH_3)NHCOCH_3$(*m'*,*p'*-).—3-Methyl-4-acetamino-chloroacetyl-benzyl amine[1] yielded a reaction mixture which set to a gelatinous mass on cooling. This was broken up, filtered, and washed first with 50% alcohol, then with water. In order to obtain the acid in crystalline form it was found necessary to pass through the *sodium salt*, a process which caused a great reduction in the yield. The amorphous product was first partly purified by solution in dil. sodium hydroxide and reprecipitation with acetic acid. After filtering and washing, the precipitate was dissolved in a small volume of dil. sodium hydroxide solution, carefully neutralized with acetic acid, and treated with a large volume of absolute alcohol. On standing in the refrigerator the sodium salt separated as a voluminous, almost gelatinous mass of delicate, microscopic needles. This was filtered off, recrystallized from 85% alcohol, and air-dried.

The analysis of this salt indicated that the air-dry product contained 6 molecules of water of crystallization, of which only 4.5 molecules were removed at 100° *in vacuo* over sulfuric acid.

Subs., air-dry, 0.7383: loss, 0.1053 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{18}H_{21}O_6N_3AsNa.6H_2O$: 4.5 H_2O, 14.32. Found: 14.26.

Subs., dried, 0.1214: 9.5 cc. N (26.5°, 751 mm.). Subs., 0.3410: $Mg_2As_2O_7$, 0.1109.

Calc. for $C_{18}H_{21}O_6N_3AsNa.1.5H_2O$: N, 8.68, As, 15.48. Found: N, 8.81, As, 15.70.

On treating the solution of the sodium salt with acetic acid the *arsonic acid* deposited slowly and was obtained as aggregates of flat, minute needles on recrystallization from 50% alcohol. When rapidly heated it decomposes at 278° and is soluble in boiling water and boiling 50% alcohol.

Subs., 0.1422: 11.7 cc. N (21.5°, 756 mm.).

Calc. for $C_{18}H_{22}O_6N_3As$: N, 9.66. Found: 9.49.

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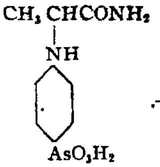
[1] *J. Biol. Chem.*, **20,** 688 (1915).

N-(Phenyl-4-arsonic Acid)-α-amino-propionamide, .—



22 g. of arsanilic acid dissolved in 100 cc. of N sodium hydroxide solution, and 22 g. of α-bromo-propionamide were boiled for $^3/_4$ hour. The arsonic acid separated on cooling. 40 cc of 10% hydrochloric acid were added to hold unchanged arsanilic acid in solution and the crystals filtered off and washed. After reprecipitating the solution of the acid in dil sodium hydroxide with acetic acid 18 g. were obtained. The amide is appreciably soluble in water at room temperature and readily on boiling, crystallizing on cooling as long, thin, hexagonal plates. It is also soluble in hot 50% alcohol When rapidly heated it darkens above 255° and decomposes at 262–3 5°.

Subs , 0 1526 12 75 cc N (22 5°, 765 mm) Subs , 0 2981 Mg_2As_2O , 0 1595
Calc for $C_9H_{13}O_4N_2As$ N, 9 73, As, 26 00 Found N, 9 72, As, 25 81

Sodium Salt—A neutral solution of the acid in dil sodium hydroxide was concentrated to dryness *in vacuo* and the residue dissolved in boiling 95% alcohol On standing in the refrigerator the salt separated from the filtered solution as long, flat, microscopic needles, which contained approximately 2 5 molecules of water of crystallization after air drying.

Subs , air-dry, 0 5718 loss, 0 0761 *in vacuo* at 100° over H_2SO_4
Calc for $C_9H_{12}O_4N_2AsNa$ 2 $5H_2O$ H_2O 12 68 Found 13 31
Subs , anhydrous, 0 1443 11 00 cc N (20 5°, 765 mm) Subs , 0 3333 $Mg_2As_2O_7$, 0 1643
Calc for $C_9H_{12}O_4N_2AsNa$ N, 9 03, As, 24 16 Found N, 8 93, As, 23 79

Oxanilamide-*p*-arsonic acid (*p*-oxamylamino-phenylarsonic acid), p-$H_2O_3AsC_6H_4NHCOCONH_2$—This substance, although not a glycine derivative, was suggested by its analogy to phenylglycineamide-*p*-arsonic acid, and is, therefore, described here for lack of a more appropriate place. 5 g. of anhydrous sodium arsanilate and 10 g of ethyl oxamate were heated for 2 hours at 140–50°. The mixture was digested with water, very little going into solution, then acidified with acetic acid and filtered and washed with water. The crude mass was dissolved in dil. ammonia, and on acidifying the warm filtrate with acetic acid the substance slowly recystallized as felted masses of minute needles in a yield of 2.5 g. It does not darken or melt when heated to 280° and is very sparingly soluble in boiling water of 50% alcohol The solution in dil. sodium hydroxide evolves ammonia on boiling.

Subs , 0 1546 12 8 cc N (22 5°, 761 mm). Subs , 0 3022 $Mg_2As_2O_7$, 0.1613
Calc. for $C_8H_9O_5N_2As$ N, 9 73, As, 26 01 Found N, 9 58, As, 25 76

(B) Derivatives of *o*- and *m*-Aminophenylarsonic Acids.

***N*-(Phenyl-2-arsonic acid)glycine-amide.**—8.8 g. of *o*-aminophenyl-arsonic acid (*o*-arsanilic acid)[1] dissolved in 40 cc. of *N* sodium hydroxide solution and 7.5 g. of chloroacetamide yielded after $^3/_4$ of an hour the glycine-amide, which crystallized on cooling. The mixture was acidified to congo red with hydrochloric acid and allowed to separate more completely in the refrigerator overnight. After filtration and washing with cold water it was dissolved in a small volume of dil ammonia and acidified to congo red with hydrochloric acid. On standing in the ice-box the arsonic acid separated as flat, microscopic needles. The yield was 5 g. In contradistinction to the *meta* and *para* isomers the *ortho* acid is not displaced completely from its salts by so weak an acid as acetic acid The substance is soluble in hot 50% alcohol and boiling water and separates from the latter as sheaves of long, thin, narrow plates. It is sparingly soluble in hot methyl and ethyl alcohols When rapidly heated it decomposes at 198–9°.

Subs., 0.1405 12.2 cc N (23.5°, 756 mm.) Subs., 0.2451 $Mg_2As_2O_7$, 0.1372

Calc. for $C_8H_{11}O_4N_2As$ N, 10.22, As, 27.33 Found N, 9.96, As, 27.00

***N*-(Phenyl-3-arsonic acid)glycineamide.**—A solution of 25 g of *m*-arsanilic acid[1] in 115 cc. of *N* sodium hydroxide solution, and 21 g. of chloroacetamide were boiled for 45 minutes. On standing in the refrigerator the clear solution gradually deposited the reaction product as a hard crust of aggregates of needles which were contaminated with unchanged chloroacetamide. On stirring and rubbing crystallization rapidly completed itself. The substance was filtered off, washed with ice water and dried. The powdered substance was leached out with dry acetone to remove chloroacetamide and then recrystallized from a small volume of hot water. It separated slowly as aggregates of prismatic needles in a yield of 18.5 g. When rapidly heated to 170° and then slowly the substance melts at 175–7° to a liquid filled with bubbles. It is quite soluble in cold water and very easily so on warming. It is also readily soluble in hot ethyl or methyl alcohol, or glacial acetic acid, but practically insoluble in hot acetone.

Subs., 0.1334 11.8 cc N (24.0°, 765 mm.) Subs., 0.3146 $Mg_2As_2O_7$, 0.1783

Calc. for $C_8H_{11}O_4N_2As$ N, 10.22, As, 27.33 Found N, 10.23; As, 27.42

***N*-(Phenyl-3-arsonic acid)glycine methyl amide.**—12 g. of chloro-acetyl-methylamine[2] yielded after one hour's boiling a mixture from which the methyl amide separated slowly on cooling and scratching. On recrystallizing from hot water, in which it is readily soluble, it separated as aggregates of flat, microscopic needles or platelets. The yield was 13.8 g. The substance is sparingly soluble in cold water or 50%

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[1] This Journal, 40, 1583 (1918).

[2] *Ibid.*, 41, 472 (1919).

alcohol, readily on warming. When rapidly heated it darkens and melts at 193–4.5° with gas evolution.

Subs., 0.1452: 12.45 cc. N (22.5°, 753 mm.). Subs., 0.3659: $Mg_2As_2O_7$, 0.1986.
Calc. for $C_9H_{13}O_4N_2As$. N, 9.73; As, 26.00. Found N, 9.82; As, 26.21.

(C) Derivatives of Aminotolylarsonic Acids.

***N*-(2-Methylphenyl-5-arsonic acid)glycineamide.**—After one hour's boiling the product from 4.6 g. of 3-amino-4-methylphenyl arsonic acid[1] and 3.8 g. of chloroacetamide slowly crystallized on cooling and acidifying with hydrochloric acid. Reprecipitated from ammoniacal solution by acetic acid it separates slowly as delicate, interlaced needles which do not melt below 285°. It is sparingly soluble in water, alcohol or acetic acid in the cold, but readily on warming. Methyl alcohol dissolves the substance at room temperature.

Subs., 0.1702. (Kjeldahl) 11.65 cc. 0.1 *N* HCl. Subs., 0.2520: $Mg_2As_2O_7$, 0.1347.
Calc. for $C_9H_{13}O_4N_2As$: N, 9.73; As, 26.00. Found: N, 9.59; As, 25.79.

***N*-(2-Methylphenyl-4-arsonic acid)glycineamide.**—As in the preceding case 23 g. of 1-amino-2-methylphenyl-4-arsonic acid (from *o*-toluidine) and 19 g. of chloroacetamide yielded the glycinamide. This was purified by solution in dil. ammonia and re-precipitation with acetic acid, separating as aggregates of glistening platelets which darken above 250° and decompose at about 283°. The yield was 10 g. The substance is sparingly soluble in boiling water but more readily so in boiling 50% alcohol.

Subs., 0.1417: 12.00 cc. N (22.5°, 756 mm.). Subs., 0.2619: $Mg_2As_2O_7$, 0.1393.
Calc. for $C_9H_{13}O_4N_2As$: N, 9.73; As, 26.00. Found: N, 9.74; As, 25.67.

***N*-(3 Methylphenyl-4-arsonic acid)glycineamide.**—This substance was prepared in similar manner from 1-amino-3-methylphenyl-4-arsonic acid.[2] The amide is soluble in boiling water, from which it separates as lustrous, diamond-shaped platelets. It is also soluble in boiling 50% alcohol and melts at 203–5° with gas evolution.

Subs., 0.1384: 11.8 cc. N (21.0°, 757 mm.). Subs., 0.3120; $Mg_2As_2O_7$, 0.1668.
Calc. for $C_9H_{13}O_4N_2As$: N, 9.73; As, 26.00. Found: N, 9.87; As, 25.81.

***N*-(2,5-Dimethylphenyl-4-arsonic acid)glycineamide.**—2,5-Dimethyl-4-aminophenyl arsonic acid[3] dissolved in *N* sodium hydroxide solution was boiled for 45 minutes with 2 g. of chloroacetamide. On acidifying to congo red with hydrochloric acid and cooling, the arsonic acid crystallized. The crude product was dissolved in dil. ammonia, treated with boneblack, and the filtrate acidified with acetic acid, the arsonic acid separating slowly as aggregates of slightly brownish plates and prisms. When rapidly heated it melts and decomposes at 236–7° with preliminary darkening and softening. It is sparingly soluble in cold water, acetic acid, or 50% alcohol, but dissolves more easily in these solvents on boiling.

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[1] THIS JOURNAL, 40, 1586 (1918).

[2] *Ibid.*, 40, 1588 (1918).

[3] *Ibid.*, 40, 1590 (1918).

Subs., 0.1644: (Kjeldahl) 10.9 cc. 0.1 *N* HCl. Subs., 0.3224: $Mg_2As_2O_7$, 0.1644.
Calc. for $C_{10}H_{15}O_4N_2As$: N, 9.27; As, 24.81. Found: N, 9.29; As, 24.61.

NEW YORK, N. Y.

[CONTRIBUTION FROM THE LABORATORIES OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH.]

AROMATIC ARSENIC COMPOUNDS. III. THE UREIDES AND β-SUBSTITUTED UREIDES OF *N*-ARYLGLYCINE ARSONIC ACIDS.

BY WALTER A. JACOBS AND MICHAEL HEIDELBERGER.

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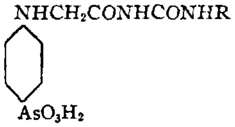
On replacing the amides of chloroacetic acid by the ureide and its β-alkyl or -aryl derivatives in the reaction described in the preceding paper, the ureides and substituted ureides of the arylglycine arsonic acids were obtained,



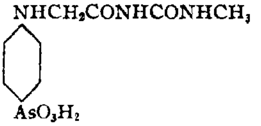
$$NHCH_2CONHCONHR-C_6H_4-AsO_3H_2$$

in which R may be hydrogen, an alkyl, or an aryl radical.

When chloroacetyl-urea or its simpler β-alkyl derivatives were employed the reaction could be accomplished by boiling in aqueous solution with the sodium salt of the aminoaryl arsonic acid. In the preparation of the β-arylureides of phenylglycine arsonic acid, however, involving the use of the very sparingly soluble chloroacetyl-substituted phenyl-ureas, the reaction proceeded most satisfactorily in 50% alcohol and only after sodium iodide had been added in order to cause the intermediate formation of the more reactive iodoacetyl compounds.

The new arsonic acids of this series resemble in their general properties the amides of the arylglycine arsonic acids, forming colorless crystalline compounds which are on the whole less soluble than the corresponding substances in the amide series. Like the latter they form stable and soluble neutral salts with the alkali metals. The ureide linkage, like that of the amides, is easily ruptured, this often occurring even at room temperature in solutions containing excess fixed alkali. Therefore, it was found important to avoid undue exposure to such conditions during the manipulations employed for the preparation of the sodium salts or in the purification of the acids by solution in alkali and reprecipitation with acids. In the latter case the use of dil. ammonia avoided this danger.

Of the numerous substances of this group which were prepared and studied the methylureide of *N*-phenylglycine-*p*-arsonic acid



has been of special interest since it has been found to exert a definite therapeutic effect in experimental syphilis and trypanosomiasis in rabbits.[1] Interesting biological results were also obtained with the ureide itself, although less striking than those given by the methyl derivative. The biological data will be published elsewhere by Drs. Brown and Pearce.

EXPERIMENTAL.

(A) Derivatives of *p*-Arsanilic Acid.

***N*-(Phenyl-4-arsonic acid)glycine-ureide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHCONH_2$.—44 g. of arsanilic acid, dissolved in 200 cc. of *N* sodium hydroxide solution, and 27 g. of chloroacetyl-urea were boiled under a reflux condenser. After about 15 minutes the reaction product separated. The mixture was heated in a water bath for $^3/_4$ of an hour longer, cooled, and treated with 50 cc. of conc. hydrochloric acid. The crude, washed ureide was dissolved in dil. ammonia and reprecipitated with acetic acid, separating as aggregates of microscopic needles. It is sparingly soluble in boiling water or 50% alcohol and almost insoluble in methyl alcohol. When rapidly heated it sinters slightly above 230° and darkens, but does not melt below 280°

Subs., 0.2959 (Kjeldahl) 27.7 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1445.
Calc. for $C_9H_{12}O_6N_3As$: N, 13.25; As, 23.62. Found: N, 13.12; As, 23.56.

Sodium Salt.—The crude acid obtained above was suspended in a small volume of water and carefully treated with sodium hydroxide until solution was complete and the reaction was neutral to litmus. Addition of too much alkali is to be avoided owing to the danger of hydrolysis. An equal volume of saturated sodium acetate solution was then added, the sodium salt of the arsonic acid separating as well defined hexagonal or diamond-shaped, microscopic platelets. After standing in the refrigerator, the salt was filtered off, washed with a little ice water, and recrystallized from a small volume of hot water. The air-dried salt contains two molecules of water of crystallization and is readily soluble in water. The yield was 30 g. An additional quantity of the arsonic acid was contained in the mother liquors.

Subs., air-dry, 0.3724: loss, 0.0355 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_9H_{11}O_6N_3AsNa.2H_2O$: H_2O, 9.60. Found: 9.53.
Subs., anhydrous, 0.2968: (Kjeldahl) 25.8 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1372.
Calc. for $C_9H_{11}O_6N_3AsNa$: N, 12.39; As, 22.09. Found: N, 12.18; As, 22.31.

Solutions of the sodium salt give precipitates with salts of the heavy metals. The *silver salt* forms colorless, microscopic needles. Magnesia mixture does not precipitate the solution in the cold but the *magnesium salt* separates on boiling.

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[1] Cf. footnote, THIS JOURNAL, 41, 1588–9 (1919).

N-**(Phenyl-4-arsonic acid) glycine-methylureide,** *p*-$H_2O_3AsC_6H_4NH$-$CH_2CONHCONHCH_3$.—44 g. of arsanilic acid were dissolved in 200 cc. of *N* sodium hydroxide solution and 30 g of α-chloroacetyl-β-methyl urea added. The mixture was boiled for one hour, during which the sparingly soluble chloro compound gradually dissolved. The ureide crystallized on cooling, or in some cases during the heating, after which the mixture was acidified to congo red with hydrochloric acid and filtered. The crude substance was dissolved in dil. ammonia and precipitated by acidifying the solution with acetic acid, but this did not always give satisfactory analytical figures. In order to obtain the acid pure it was converted into the sodium salt as described below and this dissolved in water and again acidified with acetic acid. The substance is sparingly soluble in hot water, separating on cooling as long, thin, glistening needles It is also difficultly soluble in boiling 50% alcohol and is practically insoluble in the usual organic solvents. When rapidly heated to 220°, then slowly, it decomposes at 224–5°

Subs, 0 1507 (Kjeldahl) 13 5 cc 0 1 *N* HCl Subs, 0 3428. Mg_2As_2O, 0 1590

Calc for $C_{10}H_{14}O_5N_3As$ N, 12 69; As, 22 63 Found N, 12 54, As, 22 40

Sodium Salt.—The acid was suspended in a small volume of hot water and carefully treated with sodium hydroxide until the solution reacted neutral to litmus, carefully avoiding an excess of alkali owing to the danger of saponification. After filtering and cooling the sodium salt slowly crystallized and after thorough chilling the salt was filtered off and washed with ice water It was recrystallized from a small volume of water and air dried. The yield was 30 g. The sodium salt separates from water as microscopic platelets containing 7 molecules of water of crystallization, although slight impurities, or the conditions under which it is obtained, are apt to affect the water content. It is quite readily soluble in water, exceptionally so on warming, and easily forms supersaturated solutions. The solution of the sodium salt is not precipitated by magnesia mixture in the cold, but yields a precipitate of the *magnesium salt* on boiling. Heavy metal salts cause insoluble precipitates, the *silver salt* separating as thin, microscopic platelets.

Subs, air-dry, 0 7551 loss, 0 2013 *in vacuo* at 100° over H_2SO_4

Calc for $C_{10}H_{13}O_5N_3AsNa\ 7H_2O$ H_2O, 26 30 Found 26 66

Subs, anhydrous, 0 1438 15 0 cc N (24 5°, 754 mm) Subs, 0 3041 $Mg_2As_2O_7$, 0 1346

Calc. for $C_{10}H_{13}O_5N_3AsNa$· N, 11 89, As, 21 22 Found N, 12 04, As, 21 35

N-**(Phenyl-4-arsonic acid)glycine-ethylureide,** *p*-$H_2O_3AsC_6H_4NHCH_2$-$CONHCONHC_2H_5$—Treated as described in the case of the methylureide, 3 3 g. of α-chloroacetyl-β-ethyl-urea[1] yielded 4.5 g. of the ethylureide arsonic acid. The substance is precipitated from the hot solution of its sodium salt (see below) by acetic acid as plumes of microscopic needles which are very difficultly soluble in hot water or methyl alcohol but more readily so in 50% alcohol. When rapidly heated to 220°, then slowly, it decomposes at 223–5°.

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[1] THIS JOURNAL, 41, 473 (1919).

Subs., 0.1415: 15.0 cc. N (26.5°, 757 mm.).
Calc. for $C_{11}H_{16}O_5N_3As$: N, 12.17. Found: 12.03.

Sodium Salt.—An exactly neutral solution of the acid in a small volume of sodium hydroxide solution was treated with several volumes of alcohol. On scratching the salt rapidly separated as a paste of thin, microscopic platelets which were recrystallized from hot 85% alcohol and air dried. As so obtained the salt contained approximately 4.5 molecules of water of crystallization and dissolved readily in water.

Subs, air-dry, 1.0813: loss, 0.1892 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{11}H_{15}O_5N_3AsNa.4.5H_2O$: H_2O, 18.08. Found: 17.50.
Subs., anhydrous, 0.2950: (Kjeldahl) 23.7 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1235.
Calc. for $C_{11}H_{15}O_5N_3AsNa$: N, 11.45; As, 20.42. Found: N, 11.26; As, 20.21.

N-**(Phenyl-4-arsonic acid)glycine-benzylureide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHCONHCH_2C_6H_5$.—4.4 g. of arsanilic acid were dissolved in 20 cc. of *N* sodium hydroxide solution and 4.6 g. of α-chloroacetyl-β-benzyl urea[1] and 20 cc. of alcohol were added. After 3 hours' boiling, solution was complete and the mixture was chilled, diluted with water, and treated with a slight excess of ammonia. Some insoluble material was filtered off and the filtrate acidified with acetic acid, the benzylureide separating at once. For purification it was again dissolved in dil. ammonia and precipitated by acetic acid. The yield was 2.5 g. Recrystallized from 50% alcohol the acid separated as rosets of delicate needles which, when rapidly heated to 220° and then slowly, decompose at 225°. It is sparingly soluble in boiling water and practically insoluble in methyl alcohol.

Subs., 0.3184: (Kjeldahl) 23.6 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1205
Calc. for $C_{16}H_{18}O_5N_3As$: N, 10.32; As, 18.39. Found: N, 10.38; As, 18.26.

α-*N*-**(Phenyl-4-arsonic acid)aminopropionyl-urea,** *p*-$H_2O_3AsC_6H_4NHCH(CH_3)CONHCONH_2$.—8.8 g. of arsanilic acid dissolved in 40 cc. of *N* sodium hydroxide solution, and 8 g. of α-bromopropionyl-urea were boiled for one hour. The urea gradually dissolved and the arsonic acid rapidly crystallized on cooling, after which the mixture was treated with 20 cc. of 10% hydrochloric acid and filtered. The resulting substance was reprecipitated from its ammoniacal solution by acetic acid in a yield of 7 g. Recrystallized from 50% alcohol it forms aggregates of minute needles which are sparingly soluble in water and methyl alcohol. When rapidly heated to 220°, then slowly, it decomposes at 225–6°.

Subs., 0.1512: 16.7 cc. N (28.0°, 761 mm.). Subs., 0.3142: $Mg_2As_2O_7$, 0.1475.
Calc. for $C_{10}H_{14}O_5N_3As$: N, 12.69; As, 22.63. Found: N, 12.55; As, 22.65.

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[1] *J. Biol. Chem.*, 21, 152 (1915).

N-(Phenyl-4-arsonic acid)glycine-phenylureide, p-$H_2O_3AsC_6H_4NH$-$CH_2CONHCONHC_6H_5$.—4.4 g. of arsanilic acid were dissolved in 20 cc. of N sodium hydroxide solution and 4.4 g. of chloroacetyl-phenyl-urea, 4 g. of sodium iodide, and 40 cc. of alcohol were added. After 4 hours' boiling the reaction product was filtered off and dissolved in dil. ammonia. The filtered solution was heated and then treated with an excess of acetic acid, causing the separation of the arsonic acid as feathery aggregates of silky hairs. When rapidly heated to 280° the acid darkens slightly and then melts. It is appreciably soluble in boiling 50% alcohol, separating on cooling as long, fine needles, and is almost insoluble in boiling water or methyl alcohol.

Subs., 0.1422: 13.25 cc. N (19.0°, 749 mm.).
Calc. for $C_{15}H_{16}O_6N_3As$: N, 10.69. Found: 10.73.

Sodium Salt.—The acid was suspended in a small amount of hot water and carefully treated with sodium hydroxide solution until just dissolved. The sodium salt separated on cooling as lustrous leaflets. The crystallization was aided by the addition of saturated sodium acetate solution. After filtration and washing with ice water the salt was recrystallized from 50% alcohol, separating on cooling as flat needles containing 5 molecules of water of crystallization.

Subs., air-dry, 0.9424: loss, 0.1701 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{15}H_{15}O_6N_3AsNa.5H_2O$. H_2O, 17.83. Found. 18.05.
Subs., anhydrous, 0.3318: (Kjeldahl) 23.9 cc. 0.1 N HCl; $Mg_2As_2O_7$, 0.1251.
Calc. for $C_{15}H_{15}O_6N_3AsNa$. N, 10.13; As, 18.06. Found. N, 10.09; As, 18.20.

N-(Phenyl-4-arsonic acid)glycine-4′-acetamino-phenylureide, p-$H_2O_3AsC_6H_4NHCH_2CONHCONHC_6H_4NHCOCH_3(p\text{-})$.—On boiling 4.4 g. of arsanilic acid dissolved in 20 cc. of N sodium hydroxide solution and 20 cc. of alcohol with 5.4 g. of p-acetaminophenyl-chloroacetyl-urea[1] and 4 g. of sodium iodide the sparingly soluble halide was gradually replaced by the reaction product. After 4 hours the solid was almost completely soluble in dil. ammonia, and was then filtered off, dissolved in hot dil. ammonia and precipitated from the hot solution by acetic acid. The arsonic acid separated quickly in clusters of flat, microscopic needles which sinter and darken above 240° when rapidly heated and decompose at 265–6°. The acid is almost insoluble in boiling water but is appreciably soluble in hot 50% alcohol, separating on cooling as plumes of long, delicate hairs.

Subs., 0.1654 (Kjeldahl) 14.65 cc. 0.1 N HCl.
Calc. for $C_{17}H_{19}O_6N_4As$. N, 12.44. Found: 12.41.

Sodium Salt.—A concentrated neutral solution of the acid in dil. sodium hydroxide was salted out by the addition of saturated sodium acetate solution and recrystallized from a small volume of boiling water to which a few drops of sodium carbonate solution were added in order to prevent the slight hydrolysis of the salt and separation of the acid which otherwise occurred in the hot solution. The salt separated on chilling as woolly masses of flat needles which contained 5 molecules of water of crystallization.

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[1] THIS JOURNAL, 39, 1455 (1917).

Subs., air-dry, 0 6962 loss, 0 1114 *in vacuo* at 100° over H_2SO_4
Calc. for $C_{17}H_{18}O_6N_4AsNa\ 5H_2O$ H_2O, 16 02 Found 16 00
Subs., anhydrous, 0 3165 (Kjeldahl) 26 7 cc 0 1 *N* HCl, $Mg_2As_2O_7$, 0 1028.
Calc. for $C_{17}H_{18}O_6N_4AsNa$ N, 11 87, As, 15 88 Found N, 11 82; As, 15.68.

N-**(Phenyl-4-arsonic acid)glycine-3′-oxyamylamino-phenylureide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHCONHC_6H_4NHCOCONH_2$(*m*).— 4.4 g. of arsanilic acid were dissolved in 20 cc. of *N* sodium hydroxide solution and 40 cc. of alcohol and boiled with 4.4 g. of sodium iodide and 6.2 g. of *m*-chloroacetyl-uramino-oxanilamide,[1] the sparingly soluble halide being gradually replaced by the reaction product. After 6 hours the solid was filtered off and digested with dil. ammonia. The filtrate from the undissolved material was diluted to 500 cc, heated on the water bath, and treated with an excess of acetic acid. Precipitated in this manner from the hot solution the arsonic acid separated as a micro-crystalline powder which was easily filtered. The yield was 1 3 g. Although almost insoluble in boiling water the acid dissolves appreciably in hot 50% alcohol. When rapidly heated it decomposes at 223–4°.

Subs, 0 1172· 15 2 cc N (23 5°, 747 mm) Subs, 0 2563 $Mg_2As_2O_7$, 0.0819.
Calc. for $C_{17}H_{18}O\ N_6As$ N, 14 62, As, 15 64 Found N, 14 68, As, 15.42.

N-**(Phenyl-4-arsonic acid)glycine-4′-hydroxyphenylureide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHCONHC_6H_4OH$(*p*-)—Because of our inability to prepare satisfactorily *p*-hydroxyphenyl-chloroacetyl-urea the arsonic acid was obtained by using the acetate of this substance. 2 2 g. of arsanilic acid were dissolved in 10 cc. of *N* sodium hydroxide solution and boiled for 2 hours with 2.7 g. of *p*-acetoxyphenyl-chloroacetyl-urea,[2] 2 g. of sodium iodide and 20 cc. of alcohol. On cooling the mixture set to a crystalline cake which was disintegrated, filtered, and washed with 50% alcohol. This product, in which the acetoxy group was presumably still intact, was dissolved in cold, dil. sodium hydroxide solution, making definitely alkaline to phenolphthalein in order to saponify the ester group. The solution was immediately filtered and exactly neutralized with acetic acid, for if allowed to stand too long in alkaline solution the glycylurea grouping is apt to be hydrolyzed as well, giving phenylglycine arsonic acid. From this solution the sodium salt described below was obtained. The acid itself was obtained by dissolving the sodium salts in hot water and treating with an excess of acetic acid, separating at once as microscopic needles containing 1.5 molecules of water of crystallization. The anhydrous substance darkens above 200° and sinters and chars at about 250° when rapidly heated, but does not melt up to 280°.

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[1] This Journal, **39**, 1453 (1917).
[2] *Ibid.*, **39**, 2441 (1917).

Subs., air-dry, 0.1851: loss, 0.0113 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{16}H_{16}O_6N_3As.1.5H_2O$: H_2O, 6.20. Found: 6.10.
Subs., anhydrous, 0.1726: (Kjeldahl) 12.80 cc. 0.1 *N* HCl.
Calc. for $C_{16}H_{16}O_6N_3As$: N, 10.27. Found: 10.38.

Sodium Salt.—This was obtained from the solution described above, crystallization being facilitated by the addition of saturated sodium acetate solution. The salt separated as nacreous plates, in a yield of only 1.3 g., owing possibly to the destruction of the substance during the saponification of the acetyl group. When recrystallized from 50% alcohol the salt separates as glistening leaflets containing from 4 to 4.5 molecules of water of crystallization. It is fairly readily soluble in water, particularly on warming.

Subs., air-dry, 0.3698: loss, 0.0560 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{16}H_{15}O_6N_3AsNa.4.5H_2O$: H_2O, 15.81. Found: 15.14.
Subs., anhydrous, 0.2937: (Kjeldahl) 20.5 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1065.
Calc. for $C_{16}H_{15}O_6N_3AsNa$: N, 9.75; As, 17.39. Found: N, 9.78; As, 17.51.

***N*-(Phenyl-4-arsonic acid)glycyl-4-uramino-phenoxyacetamide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHCONHC_6H_4OCH_2CONH_2$(*p*-).—In this case, using *p*-chloroacetyluramino phenoxyacetamide[1] as starting material the reaction mixture behaved as in the preceding examples. After 4 to 5 hours' boiling the mixture was diluted with water, filtered, and the solid suspended in water and treated carefully with dil. sodium hydroxide solution until just alkaline to litmus. The filtrate was exactly neutralized with acetic acid and the *sodium salt* thrown out by the addition of sodium acetate, filtered off, and washed with 20% sodium acetate solution, then with 85% alcohol. Recrystallized from 50% alcohol it separated as aggregates of slightly purplish plates which were practically anhydrous. The salt is fairly readily soluble in water, especially on warming.

Subs., 0.2959: (Kjeldahl) 24.95 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.0929.
Calc. for $C_{17}H_{18}O_7N_4AsNa$: N, 11.48; As, 15.36. Found: N, 11.81; As, 15.16.

On adding acetic acid to a dilute solution of the sodium salt the *arsonic acid* separates slowly as glistening, diamond-shaped platelets which are almost insoluble in boiling water or boiling 50% alcohol. When rapidly heated it decomposes at 243–4° with preliminary sintering and darkening.

Subs., 0.1546: 16.05 cc. N (16.5°, 753 mm.).
Calc. for $C_{17}H_{19}O_7N_4As$: N, 12.02. Found: 12.13.

***N*-(Phenyl-4-arsonic acid)glycyl-3-uramino-benzamide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHCONHC_6H_4CONH_2$(*m*-).—In the preparation of this substance the sparingly soluble *m*-chloroacetyluramino-benzamide[2] rapidly dissolved as the reaction progressed, and the new arsonic acid soon separated. After 2 hours' boiling the solid was dissolved in dil. ammonia, the filtrate diluted to several hundred cc., heated, and then acidified with acetic acid. The arsonic acid separated as a rather voluminous, micro-crystalline powder. 4.2 g. were obtained from 5.2 g. of halide. It is very sparingly soluble in boiling water, but somewhat more soluble in boiling 50% alcohol, from which it separates as sheaves of flat, microscopic needles. When rapidly heated it melts at 213–4° with effervescence and darkening.

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[1] THIS JOURNAL, 39, 2439 (1917).
[2] *Ibid.*, 39, 2437 (1917).

Subs., 0.1508: 17.0 cc. N (22.5°, 757 mm.). Subs., 0.3042: $Mg_2As_2O_7$, 0.1066.
Calc. for $C_{16}H_{17}O_6N_4As$: N, 12.84; As, 17.18. Found: N, 12.97; As, 16.92.

***N*-(Phenyl-4-arsonic acid)glycyl-4-uramino-benzamide.**—Starting with 5.2 g. of *p*-chloroacetyluramino-benzamide[1] the reaction mixture was boiled for 5 hours. The product obtained was dissolved in dil. ammonia, and the filtrate heated and acidified with acetic acid, the arsonic acid separating as short, microscopic needles. It was further purified by redissolving in dil. ammonia and reprecipitating with acetic acid. The yield was 3.1 g. When rapidly heated the substance darkens above 230° and decomposes at 245°.

Subs., 0.3288 (Kjeldahl): 29.85 cc. 0.1 *N* HCl, $Mg_2As_2O_7$, 0.1160.
Calc. for $C_{16}H_{17}O_6N_4As$: N, 12.84; As, 17.18. Found: N, 12.72; As, 17.03.

***N*-(Phenyl-4-arsonic acid)glycyl-3-uramino-phenylacetamide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHCONHC_6H_4CH_2CONH_2$(*m*-).—In this case the reaction mixture, containing 10.8 g. of *m*-chloroacetyluramino-phenylacetamide,[1] was boiled for 3 hours. On cooling and scratching the arsonic acid separated from the clear solution as a thick, crystalline mass. After filtering, the crude product was dissolved in dil. ammonia and the filtrate treated with acetic acid, the substance gradually separating as a thick mass of needles in a yield of 9.5 g. The arsonic acid is soluble in hot water from which it separates as felted needles. It is also soluble in 50% alcohol and, when rapidly heated, decomposes at 214–6°.

Subs., 0.1460: 15.9 cc. N (23.0°, 754 mm.). Subs., 0.3102: $Mg_2As_2O_7$, 0.1055.
Calc. for $C_{17}H_{19}O_6N_4As$: N, 12.45; As, 16.65. Found: N, 12.47; As, 16.42.

***N*-(Phenyl-4-arsonic acid)glycyl-4-uraminophenyl acetamide.**—The reaction mixture, containing 8.1 g. of *p*-chloroacetyluramino-phenylacetamide[2] yielded a clear solution after 2 hours' boiling. At the end of 4 hours the solution was cooled and the precipitated solid dissolved by the careful addition of dil. sodium hydroxide solution. After filtering and exactly neutralizing with acetic acid the *sodium salt* was salted out with sodium acetate, filtered off, washed with 85% alcohol, dissolved in a small volume of warm water and treated with an equal volume of alcohol. The sodium salt separated as microscopic, hexagonal platelets containing about 2.5 molecules of water of crystallization. The yield of the air-dry salt was 4.5 g.

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[1] THIS JOURNAL, 39, 2438 (1917).

[2] *Ibid.*, 39, 2439 (1917).

Subs., air-dry, 0.3606: loss, 0.0330 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{17}H_{18}O_6N_4AsNa.2.5H_2O$: H_2O, 8.71. Found: 9.15.

Subs., anhydrous, 0.1213: 12.8 cc. N (27.0°, 764 mm.). Subs., 0.2059: $Mg_2As_2O_7$, 0.0667.

Calc. for $C_{17}H_{18}O_6N_4AsNa$: N, 11.87; As, 15.88. Found: N, 12.08; As, 15.64.

On adding acetic acid to the hot solution of the sodium salt the *arsonic acid* separated slowly as plumes of delicate needles containing one molecule of water of crystallization. It is very sparingly soluble in boiling water but more readily so in boiling 50% alcohol. The anhydrous substance decomposes at 218–21° when rapidly heated.

Subs., air-dry, 0.6892: loss, 0.0255 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{17}H_{19}O_6N_4As.H_2O$: H_2O, 3.85. Found: 3.70.

Subs., anhydrous, 0.1485: (Kjeldahl) 13.2 cc. 0.1 *N* HCl.

Calc. for $C_{17}H_{19}O_6N_4As$: N, 12.45. Found: 12.44.

(B) Derivatives of *o*-Arsanilic Acid.

***N*-(Phenyl-2-arsonic acid) glycine-ureide.**—4.4 g. of *o*-arsanilic acid[1] were dissolved in 20 cc. of *N* sodium hydroxide solution and boiled 1/2 hour with 2.7 g. of chloroacetyl-urea, the new arsonic acid precipitating after 7 to 8 minutes. The mixture was cooled, acidified to congo red, filtered, and the solid suspended in a little water, treated with an excess of ammonia, and the solution treated with boneblack and filtered. The pale yellow filtrate, heated to boiling and acidified strongly with acetic acid, deposited the ureide as plumes of minute, delicate needles which are almost insoluble in the usual neutral solvents. The yield was 2.5 g. When rapidly heated to 230°, then slowly, it melts and decomposes at 231–2° with preliminary softening and yellowing.

Subs., 0.1535: (Kjeldahl) 14.4 cc. 0.1 *N* HCl. Subs., 0.3396: $Mg_2As_7O_7$, 0.1647.

Calc. for $C_9H_{12}O_5N_3As$: N, 13.25; As, 23.62. Found: N, 13.14; As, 23.41.

***N*-(Phenyl-2-arsonic acid)-glycine-methylureide.**—A solution of 4.4 g. of *o*-arsanilic acid in 20 cc. of *N* aqueous sodium hydroxide solution was boiled 50 minutes with 3.1 g. of α-chloroacetyl-β-methyl-urea, the latter gradually dissolving and the mixture finally setting to an almost solid cake, being then transferred to the water bath and heated 1/2 hour longer. After reprecipitation from dil. ammonia in the usual manner, 2.1 g. of the arsonic acid were obtained as balls of minute needles which are very sparingly soluble in boiling water, alcohol, or methyl alcohol, but dissolve in boiling acetic acid. When rapidly heated to 215°, then slowly, the acid melts and decomposes at 218° with slight preliminary softening and darkening.

Subs., 0.1642: (Kjeldahl) 15.05 cc. 0.1 *N* HCl. Subs., 0.3248: $Mg_2As_2O_7$, 0.1507.

Calc. for $C_{10}H_{14}O_5N_3As$: N, 12.69; As, 22.63. Found: N, 12.84; As, 22.40.

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[1] This Journal, 40, 1583 (1918).

(C) Derivatives of *m*-Arsanilic Acid.

***N*-(Phenyl-3-arsonic acid)glycine-ureide.**—This substance was prepared and purified by the method of the preceding experiment, from 4.4 g. of *m*-arsanilic acid,[1] separating gradually as colorless microscopic needles frequently grouped in bundles. The yield was 2.5 g. It is soluble in boiling water and boiling 50% alcohol and separates from the former in rosets of minute needles. It decomposes at 208–9° with preliminary softening.

Subs., 0.1494: 17.2 cc. N (27.0°, 758 mm.). Subs., 0.3038: $Mg_2As_2O_7$, 0.1501.
Calc. for $C_9H_{12}O_6N_3As$: N, 13.25; As, 23.62. Found: N, 13.08; As, 23.84.

***N*-(Phenyl-3-arsonic acid)glycine-methylureide.**—Using 17.5 g. of *m*-arsanilic acid and 13 g. of α-chloroacetyl-β-methyl-urea in the usual manner, the substance suddenly separated after $^1/_2$ hour. 80 cc. of *N* hydrochloric acid solution were added on cooling and the precipitate filtered off and washed with water. The yield was 19 g. Recrystallized as in the preceding examples, the acid melts with decomposition at 213–3.5° when rapidly heated. It is rather sparingly soluble in boiling water or 50% alcohol, separating from the former as rosets of delicate needles.

Subs., 0.1460: 16.1 cc N (23.5°, 750 mm). Subs., 0.3273: $Mg_2As_2O_7$, 0.1493.
Calc. for $C_{10}H_{14}O_6N_3As$: N, 12.69; As, 22.63. Found: N, 12.54; As, 22.01.

(D) Derivatives of Substituted Arsanilic Acids.

***N*-(3-Methylphenyl-4-arsonic acid)glycine-ureide.**—16.2 g. of 3-methyl-4-aminophenyl arsonic acid (from *o*-toluidine), were dissolved in 70 cc. of *N* sodium hydroxide solution and boiled with 9.5 g. of chloroacetyl-urea. After $^1/_2$ hour the mixture suddenly crystallized and was cooled, treated with 25 cc. of 10% hydrochloric acid, filtered, and washed. The acid was dissolved in dil. ammonia, and the solution heated and acidified with acetic acid, causing the separation of the ureide as delicate needles. The yield was 11 g. The substance is sparingly soluble in boiling water or boiling 50% alcohol, and decomposes at about 235° when rapidly heated.

Subs., 0 1392: 15.5 cc. N (22.5°, 756 mm.). Subs., 0.3327: $Mg_2As_2O_7$, 0.1544.
Calc. for $C_{10}H_{14}O_6N_3As$: N, 12.69; As, 22.63. Found: N, 12.80; As, 22.40.

Sodium Salt.—The acid was suspended in a small volume of water and sodium hydroxide solution carefully added until solution was complete and the reaction was faintly alkaline to litmus. On warming the solution and adding 2 volumes of alcohol the sodium salt separated as glistening plates containing 2 molecules of water of crystallization. When recrystallized from a small volume of hot water it also separates as the same hydrate.

Subs., air-dry, 0.5114: loss, 0.0460 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{10}H_{13}O_6N_3AsNa.2H_2O$: H_2O, 9.26. Found: 9.00.

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[1] THIS JOURNAL, 40, 1583 (1918).

Subs., anhydrous, 0.1132: 11.4 cc. N (20.0°, 758 mm.). Subs., 0.2586: $Mg_2As_2O_7$, 0.1123.

Calc. for $C_{10}H_{13}O_5N_3AsNa$: N, 11.90; As, 21.22. Found. 11.71; As, 20.96.

***N*-(3-Methylphenyl-4-arsonic acid)glycine-methylureide.**—After one hour 23 g. of 3-methyl-4-aminophenyl arsonic acid as the sodium salt and 15 g. of α-chloroacetyl-β-methyl-urea yielded a solution which set to a thick, crystalline mass on cooling. This was diluted with water and treated with 40 cc. of 10% hydrochloric acid. Reprecipitated from hot dil. ammoniacal solution with acetic acid, the yield was 12 g. The substance is sparingly soluble in hot water but dissolves in boiling 50% alcohol. It separates from the former as hair-like needles and from the latter as radiating masses of minute needles. When rapidly heated it decomposes at 218–9°.

Subs., 0.1326: 14.0 cc. N (24 5°, 756 mm.). Subs., 0.3418 $Mg_2As_2O_7$, 0 1523.

Calc. for $C_{11}H_{16}O_6N_3As$· N, 12.17, As, 21 72. Found: N, 12 07; As, 21 52.

***N*-(2-Hydroxyphenyl-5-arsonic acid)glycine-ureide.**—On boiling a solution of 3.8 g. of 3-amino-4-hydroxyphenyl arsonic acid[1] in 16.5 cc. of *N* sodium hydroxide solution with 4.4 g. of chloroacetyl-urea it suddenly set to a solid, crystalline cake. After another hour on the water bath water was added and the crystalline mass disintegrated and filtered. Reprecipitated from solution in hot, dil. ammonia with acetic acid, the substance separated as flat, minute, almost colorless, glistening needles which contained between 1 and 1.5 molecules of water of crystallization. The yield was 3.3 g. When anhydrous it decomposes at 203–5°.

Subs., air-dry, 0.4214: loss, 0.0257 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_9H_{12}O_6N_3As.H_2O$. H_2O, 5.13. Found· 6.10

Subs., anhydrous, 0 2946: (Kjeldahl) 26.65 cc. 0 1 *N* HCl; $Mg_2As_2O_7$, 0 1380.

Calc. for $C_9H_{12}O_6N_3As$: N, 12.62; As, 22.50. Found N, 12 68; As, 22 61

NEW YORK, N Y

[CONTRIBUTION FROM THE LABORATORIES OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH]

AROMATIC ARSENIC COMPOUNDS. IV.

AROMATIC AMIDES OF *N*-ARYLGLYCINE ARSONIC ACIDS.

WALTER A. JACOBS AND MICHAEL HEIDELBERGER.

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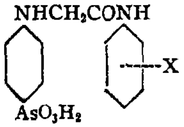
In continuation of the studies described in the preceding papers of this series,[2] we have prepared the arylamides and substituted arylamides of the arylglycine arsonic acids possessing the following general formula:



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[1] THIS JOURNAL, 40, 1590 (1918).

[2] *Ibid.*, 41, 1581, 1587, 1600 (1919).

a series of compounds with such extensive synthetic possibilities as to afford a very fertile ground for chemotherapeutic researches.[1]

Like the alkylamides and ureides these substances were readily obtained by the interaction of the sodium salt of the aminoaryl arsonic acid with the aromatic chloroacetylamino compound, according to the reaction $NaHO_3AsC_6H_4NH_2 + ClCH_2CONHAr \longrightarrow H_2O_3AsC_6H_4NHCH_2CONHAr + NaCl$. In the case of the chloroacetyl derivatives of the simpler amines or of their halogen, nitro, acylamino, carboxamide, carboxureide, or sulfonamide derivatives, the reaction was best accomplished in 50% alcoholic solution in the presence of sodium iodide, the latter causing the intermediate formation of the more reactive iodoacetyl compounds. However, where chloroacetylamino acids or the simpler chloroacetyl-aminophenols were employed the condensation could be carried out rapidly in aqueous solution without the use of sodium iodide. In such cases, one-half to one hour's boiling usually sufficed for complete reaction owing to the great lability of the chlorine in these compounds, whereas the chlorine in the first mentioned substances is far more stable. On boiling the chloroacetylamino acids or phenols with aqueous alkali or salts of weak acids a copious liberation of chlorine ion may quickly be obtained, whereas such a result can be obtained with the chloroacetyl compounds of other aromatic amines only through much more vigorous treatment.

In some instances the great reactivity of these chloroacetyl compounds produced complications, since the sodium arsanilate functioned rather as a salt of a weak acid and removed the chlorine before much opportunity for condensation with the amino group was afforded. This difficulty was overcome in the case of chloroacetyl-anthranilic acid by the use of its ethyl ester and subsequent saponification of the resulting ester arsonic acid. It was also found necessary to adopt a similar procedure in the case of chloroacetyl-methylanthranilic acid. A similar difficulty was encountered in using *o*-chloroacetylamino-phenol for the preparation of the *o*-hydroxyanilides, on account of the readiness with which it undergoes *ortho* condensation in the presence of salts of weak acids to form the anhydride of *o*-amino-phenoxyacetic acid. This reaction preponderated particularly with *o*- and *p*-arsanilic acids and only poor yields of the desired glycine compounds were obtained. The yields were greatly improved, however, by employing two molecules of arsanilic acid itself instead of the sodium salt, the formation of *o*-amino-phenoxyacetic anhydride being almost completely suppressed.

The reaction with *o*-chloroacetylamino-phenol also afforded an interesting opportunity to note the differences in reactivity between *m*-arsanilic acid on the one hand and the *o*- and *p*-acids on the other. It has been our experience that amines with negative substituents such as *m*-nitraniline react more readily with halogen-acetyl compounds than do the *o*- and *p*-isomers. In the reaction between sodium *m*-arsanilate and *o*-chloroacetylamino-phenol the tendency toward glycine formation was such as to proceed at a more rapid rate than the formation of *o*-amino-phenoxyacetic anhydride, so that the yield of the *o*-hydroxyanilide was much greater and that of the by-product much smaller than in the case of the isomeric arsanilic acids. It is probable that a comparative study of the reactivity of the aminophenyl arsonic acids with other halogen-acetyl compounds would yield a similar result. Such experiments involving velocity measurements were, however, beyond the scope of the present studies.

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[1] Cf. footnote, THIS JOURNAL, 41, 1588–9 (1919).

Special attention has been given in the present work to a study of the hydroxyanilides of the arylglycine arsonic acids, since reduction converts them into a group of arseno compounds which yield water-soluble alkali phenolates. These trivalent arsenicals have been the subject of interesting biological investigations and since both the chemical and biological studies with such compounds are still in progress, their description will be left to later communications.

As derivatives of the phenylglycine arsonic acids, the substances herein described function both as acids and bases. As acids they are easily displaced from their salts by acetic acid, except in those cases in which the arylamide nucleus is substituted by other acid groups, in which case either a mineral acid or a large excess of acetic acid is required. The feeble basic properties due to the imino group are typified by the formation of hydrochlorides only in the presence of relatively strong hydrochloric acid. As secondary amines they also yield nitroso derivatives. The amide linkage renders the glycineanilides susceptible to hydrolysis on boiling with mineral acids or alkalies, but they seem somewhat more stable toward the action of alkali than the corresponding aliphatic amides.

As a rule the free arsonic acids do not possess sharp melting or decomposition points, the values obtained depending greatly upon the rate of heating. They are on the whole but sparingly soluble in the usual solvents. The sodium salts, on the other hand, dissolve more or less readily in water depending upon the nature and position of the substituting groups and are often salted out by sodium chloride or acetate. For the convenience of biological testing the sodium salts were prepared in many cases, although this was also found a convenient means for the purification of individual compounds.

EXPERIMENTAL.

(A) Derivatives of *p*-Arsanilic Acid.

***N*-(Phenyl-4-arsonic Acid)glycineanilide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_5$.—This substance can be prepared by the two methods already described in the preparation of the amide of phenylglycine-*p*-arsonic acid;[1] *viz.*, by the reaction of sodium arsanilate with chloroacetanilide or by that of phenyl-(4-arsonic acid)-glycine methyl ester with aniline itself. Both the speed and yield of the first reaction are much improved either by replacing the chloro compound by the iodoacetyl derivative or by adding sodium iodide to the reaction mixture.

22 g. of arsanilic acid were dissolved in 100 cc. of *N* sodium hydroxide solution. To this were added 17 g. of chloroacetanilide,[2] 20 g. of sodium iodide, and 100 cc. of alcohol and the mixture was boiled for two hours. During the heating the reaction product suddenly separated. After cooling the substance was filtered off, washed with 50% alcohol and redissolved in dil. ammonia. On reprecipitating the hot solution with an excess of acetic acid, the arsonic acid separated in easily filterable form in a yield of 25 g. Recrystallized from 50% alcohol it separates as minute, delicate needles which do not melt below 285° when rapidly heated. As a secondary amine it reacts with nitrous acid, giving the nitroso derivative described below. The substance is practically insoluble in the cold in the usual organic solvents, but is appreciably dissolved by a large volume of hot methyl or ethyl alcohol or glacial acetic acid. It is insoluble in cold dil. hydrochloric acid, but on warming it dissolves, forming the hydrochloride, which separates on cooling.

Subs., 0.1308: 9 05 cc. N (22.0°, 763 mm.). Subs., 0.4164: $Mg_2As_2O_7$, 0.1828.
Calc. for $C_{14}H_{15}O_4N_2As$· N, 8.00; As, 21.39. Found· N, 8 04; As, 21.18

The substance was also prepared as follows: 6 g. of (phenyl-4-arsonic acid)-glycine methyl ester[3] and 12 g. of aniline were treated with 20 cc. of methyl alcohol and heated on the water bath until solution was complete. The alcohol was then allowed to boil off and after several hours' heating the melt began to crystallize. The residue was finally taken up in dil. sodium hydroxide solution, and made definitely alkaline to phenolphthalein to saponify any unchanged ester. The filtered solution was then acidified with acetic acid and on scratching the arsonic acid separated and was purified as above described. The substance so obtained agreed in all of its properties with that obtained by the alternative method.

Subs., 0.1549 10.6 cc. N (24.5°, 754 mm.).
Calc. for $C_{14}H_{15}O_4N_2As$. N, 8.00. Found: 7.79.

Sodium Salt.—On dissolving the arsonic acid in dil. sodium hydroxide solution until faintly alkaline to litmus and adding an equal volume of saturated sodium acetate solution, the sodium salt separated as glistening scales. After filtering and washing with 20% sodium acetate solution, and then with 85% alcohol, it was air-dried. The salt contained 4 molecules of water of crystallization. It is freely soluble in water and its dilute solutions do not give immediate precipitates with calcium or barium salts. With magnesia mixture a precipitate is formed only on heating, while heavy metal salts give insoluble precipitates at once.

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[1] THIS JOURNAL, 41, 1589 (1919).
[2] *Ibid.*, 39, 1441 (1917).
[3] *Ibid.*, 41, 1590 (1919).

Subs., air-dry, 0.9416: Loss, 0.1553 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{14}H_{14}O_4N_2AsNa.4H_2O$: H_2O, 16.22. Found 16.49.
Subs., anhydrous, 0.1709: 11.4 cc. N (21.0°, 754 mm.).
Calc. for $C_{14}H_{14}O_4N_2AsNa$: N, 7.53. Found: 7.69.

Nitroso Compound, *p*-$H_2O_3AsC_6H_4N(NO)CH_2CONHC_6H_5$.—3 g. of the arsonic acid were suspended in 35 cc. of glacial acetic acid and treated slowly, with constant agitation, with 6 cc. of a 10% sodium nitrite solution. Only a portion of the substance dissolved and the mixture was heated to boiling, forming a clear, yellow solution. To complete the reaction 0.5 cc. of sodium nitrite solution was added and the mixture cooled, rosets of flat needles forming on scratching. After dilution with water to complete the separation the nitroso compound was filtered off and recrystallized from 50% alcohol. It separated as sheaves of long, flat, colorless needles containing one molecule of water of crystallization. The yield was 2.3 g. When rapidly heated to 185°, then slowly, it effervesces at 190–2°. It is very sparingly soluble in boiling water, readily in boiling 50% alcohol, quite easily in the cold in acetic acid, and somewhat sparingly so in cold 95% alcohol. The nitroso compound is turned brown by sulfuric acid but dissolves to a colorless solution; in the presence of phenol, however, a brown solution is obtained, changing rapidly to deep green.

Subs., air-dry, 0.4429: Loss, 0.0218 *in vacuo* at 80° over H_2SO_4.
Subs., 0.1023: 9.5 cc. N (24.0°, 761 mm.). Subs., 0.2979: $Mg_2As_2O_7$, 0.1154.
Calc. for $C_{14}H_{14}O_6N_3As.H_2O$: H_2O, 4.54; N, 10.58; As, 18.87. Found: H_2O, 4.92; N, 10.69; As, 18.70.

***N*-(Phenyl-4-arsonic Acid)-glycine-2′-toluidide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4CH_3$(*o*-).—This substance was prepared as usual from chloroacetyl-*o*-toluidine, aided by the addition of sodium iodide. Purified by redissolving in a slight excess of dil. sodium hydroxide solution, warming, and reprecipitating with acetic acid the acid separated slowly as aggregates of flat, microscopic needles. Recrystallized from 50% alcohol it forms woolly masses of delicate needles which do not melt below 275° and are sparingly soluble in hot water and acetone. It is insoluble in the cold in 50 or 95% alcohol but appreciably so on boiling and readily so in hot acetic acid. It dissolves appreciably in cold methyl alcohol.

Subs., 0.2944: 9.9 cc. N (24.5°, 758 mm.).
Calc. for $C_{15}H_{17}O_4N_2As$: N, 7.69. Found: N, 7.69.

Sodium Salt.—On adding several volumes of alcohol to the neutral solution of the acid in dil. sodium hydroxide the sodium salt separates slowly as aggregates of long, narrow platelets which contain 2.5 molecules of water of crystallization.

Subs., air-dry, 0 5627. Loss, 0.0580 *in vacuo* at 100° over H_2SO_4
Calc. for $C_{15}H_{16}O_4N_2AsNa.2.5H_2O$: H_2O, 10.44. Found 10.31.
Subs., anhydrous, 0.2944: (Kjeldahl), 15.0 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1175.
Calc. for $C_{15}H_{16}O_4N_2AsNa$: N, 7.26; As, 19.41. Found: N, 7 14; As, 19.27.

N-**(Phenyl-4-arsonic Acid)-glycine-3′-toluidide.**—The yield from 3.7 g. of chloroacetyl-*m*-toluidine[1] was 4 g. The crude product was recrystallized from 85% alcohol, separating as aggregates of long, thin plates. When rapidly heated it decomposes at about 285°, with preliminary darkening and softening. It is insoluble in boiling water or acetone, but is appreciably soluble in boiling methyl and ethyl alcohols and readily so in boiling acetic acid.

Subs., 0.1929 13 3 cc. N (22.5°, 764 mm). Subs., 0.3012: $Mg_2As_2O_7$, 0.1257.
Calc for $C_{15}H_{17}O_4N_2As$ N, 7.70; As, 20 58 Found: N, 8 01; As, 20 16.

N-**(Phenyl-4-arsonic Acid)-glycine-4′-toluidide.**—This substance, obtained from chloroacetyl-*p*-toluidine, separates from the reaction mixture during the heating. Reprecipitated with acetic acid from its solution in sufficient hot. dil. sodium hydroxide it separated as minute aggregates of short, flat, microscopic needles. It crystallizes from hot 50% alcohol, in which it is but sparingly soluble, as woolly masses of minute needles which do not decompose when heated up to 280°. It is practically insoluble in boiling water, and but sparingly so in boiling methyl or ethyl alcohol but is readily soluble in boiling acetic acid.

Subs , 0.14[illegible]6: 9.8 cc. N (25.0°, 762 mm).
Calc. for $C\ H_{17}O_4N_2As$: N, 7.69. Found: 7 53

Sodium Salt.—When the acid is dissolved in hot, dil. sodium hydroxide solution and carefully neutralized with acetic acid the sodium salt separates on cooling as long, thin, curved, glistening needles, containing three molecules of water of crystallization. This salt is sparingly soluble in cold water and even less so in the presence of other sodium salts.

Subs., air-dry, 0.6936. Loss, 0.0856 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{16}H_{18}O_4N_2AsNa.3H_2O$: H_2O, 12.28. Found: 12.34.
Subs., anhydrous, 0.2989: (Kjeldahl), 15.3 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1213.
Calc. for $C_{15}H_{16}O_4N_2AsNa$: N, 7.26; As, 19.41. Found: N, 7.17; As, 19.59.

N-**(Phenyl-4-arsonic Acid)-glycine-α-naphthylamide,** *p*-$H_2O_3AsC_6H_4$-$NHCH_2CONHC_{10}H_7$(α-). — Chloroacetyl-α-naphthylamine reacted smoothly, the product separating from the clear solution on scratching. It was best purified by precipitating a hot, dil. ammoniacal solution with acetic acid, forming aggregates of microscopic needles. It is practically insoluble in boiling water or 50% alcohol. When rapidly heated it darkens slightly, but does not melt up to 280°. On heating its solution in dil. sodium hydroxide the odor of α-naphthylamine is quickly noticeable owing to slight cleavage of the amide linking.

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[1] *J. Biol. Chem.*, 21, 108 (1915).

Subs., 0.1466: 9.0 cc *N* (22.0°, 758 mm.). Subs., 0.3799: $Mg_2As_2O_7$, 0.1457.
Calc. for $C_{18}H_{17}O_4N_2As$: N, 7.00; As, 18.73. Found. N, 7.09; As, 18.51.

N-**(Phenyl-4-arsonic Acid)-glycine-β-naphthylamide.**—During the interaction of chloroacetyl-β-naphthylamine with sodium arsanilate in the presence of sodium iodide the sparingly soluble chloro compound was gradually replaced by the reaction product, so that complete solution never occurred. After 4 hours' heating the mixture was diluted with water and treated with ammonia until definitely alkaline. The filtrate was warmed and treated with acetic acid, causing the precipitation of the arsonic acid as a crystalline powder. The yield from 4.4 g. of chloro compound was 5 g. For purification it was redissolved in dil. ammonia and reprecipitated with acetic acid, forming aggregates of microscopic needles which are practically insoluble in boiling water or 50% alcohol. When rapidly heated it decomposes at 285–6° to a red liquid.

Subs., 0.2154: (Kjeldahl), 10.6 cc. 0.1 *N* HCl
Calc. for $C_{18}H_{17}O_4N_2As$: N, 7.00. Found: 6.90.

Sodium Salt.—When the acid is dissolved in warm, dil. sodium hydroxide solution and carefully neutralized with acetic acid the sparingly soluble sodium salt quickly separates as a lustrous, crystalline mass. Recrystallized from a small volume of 50% alcohol it forms aggregates of flat needles which contain approximately 4.5 molecules of water of crystallization.

Subs., air-dry, 0.8419: Loss, 0.1338 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{18}H_{16}O_4N_2AsNa.4.5H_2O$: H_2O, 16.11. Found: 15.89.
Subs., anhydrous, 0.3273: (Kjeldahl), 15.55 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1214.
Calc. for $C_{18}H_{16}O_4N_2AsNa$: N, 6.64; As, 17.74. Found: N, 6.66; As, 17.90.

N-**(Phenyl-4-arsonic Acid)-glycinediphenylamide,** *p*-$H_2O_3AsC_6H_4NHCH_2CON(C_6H_5)_2$.—On boiling equivalent amounts of sodium arsanilate, chloroacetyldiphenylamine,[1] and sodium iodide in 50% alcohol as in previous examples, an oily reaction product separated after several minutes. On continued boiling this redissolved and after about an hour the crystalline arsonic acid was deposited. The isolated product was dissolved in dil. ammonia, leaving an insoluble residue which was collected with boneblack and filtered off. On acidifying the filtrate to congo red with hydrochloric acid the diphenylamide was obtained and for final purification was redissolved in hot, very dil. ammonia and precipitated with acetic acid. The arsonic acid separated as long, thin, microscopic leaflets which contained one molecule of water of crystallization. The anhydrous substance decomposes at 271–2° with slight preliminary softening and is very sparingly soluble in boiling water or 50% alcohol.

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[1] H. Frerichs, *Chem. Zentr.*, 74, 103–4 (1903).

Subs., air-dry, 0.6797: Loss, 0.0267 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{20}H_{19}O_4N_2As.H_2O$. H_2O, 4.06. Found: 3.93

Subs., anhydrous, 0.1780: (Kjeldahl), 8.3 cc. 0.1 *N* HCl. Subs., 0.2355: $Mg_2As_2O_7$, 0.0853.

Calc. for $C_{20}H_{19}O_4N_2As$. N, 6.57; As, 17 58. Found. N, 6.53; As, 17.48.

N-**(Phenyl-4-arsonic Acid)-glycine-4′-chloroanilide,** *p*-$H_2O_3AsC_6H_4$-$NHCH_2CONHC_6H_4Cl$(*p*-).—Precipitated from the hot solution of its sodium salt with acetic acid, the substance obtained from chloroacetyl-*p*-chloroaniline quickly separates as toothed, microscopic leaflets which are often cross-shaped. It does not melt below 280° and is almost insoluble in boiling water or 50% alcohol. The sodium salt is easily salted out from its solutions by sodium acetate.

Subs., 0.3058: (Kjeldahl , 15 5 cc. 0 1 *N* HCl; $Mg_2As_2O_7$, 0.1238.

Calc. for $C_{14}H_{14}O_4N_2ClAs$ N, 7 29; As, 19 49 Found N, 7 10, As, 19.54.

N-**(Phenyl-4-arsonic Acid)glycine-4′-iodoanilide.**—(From chloroacetyl-*p*-iodoaniline.[1]) When added to the hot solution of its sodium salt, acetic acid causes the separation of the arsonic acid as broad, minute needles which do not melt below 275° and are practically insoluble in boiling water.

Subs., 0 2066 (Kjeldahl), 8 45 cc 0.1 *N* HCl.

Calc. for $C_{14}H_{14}O_4N_2IAs$ N, 5 89. Found. 5.73.

Sodium Salt.—When an aqueous suspension of the acid was neutralized with sodium hydroxide and treated with sodium acetate solution the sodium salt crystallized as glistening leaflets. Recrystallized from 85% alcohol the salt separated in rosets of needles which contained 3.5 molecules of water of crystallization.

Subs., air-dry, 0.4029. Loss, 0.0448 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{14}H_{13}O_4N_2IAsNa.3.5H_2O$. H_2O, 11.23. Found. 11.12.

Subs., anhydrous, 0.2946: (Kjeldahl), 11.65 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0 0922.

Calc. for $C_{14}H_{13}O_4N_2IAsNa$: N, 5.63; As, 15.05. Found: N, 5.54; As, 15.11.

N-**(Phenyl-4-arsonic Acid)-glycine-4′-nitroanilide,** *p*-$H_2O_3AsC_6H_4$-$NHCH_2CONHC_6H_4NO_2$(*p*-).—In this case the sparingly soluble chloroacetyl-*p*-nitraniline[2] was gradually replaced by the reaction product. The crude substance was suspended in a large volume of hot water and treated with a slight excess of ammonia. The hot, filtered solution was then treated with an excess of hydrochloric acid, causing the precipitation of the arsonic acid as long, thin, faintly yellow needles. Acetic acid is not a sufficiently strong acid completely to displace the nitro acid from its ammonium salt, and as this is also sparingly soluble in water it contaminates the free arsonic acid unless a mineral acid is used as precipitant. The yield from 14.5 g. of chloroacetyl-*p*-nitraniline was 18.5 g. The arsonic acid is practically insoluble in boiling water or 50% alcohol and does not melt below 285°.

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[1] This Journal, 39, 1441 (1917).

[2] *J. Biol. Chem.*, 21, 112 (1915).

Subs., 0 1217 11 25 cc N (27 0°, 762 mm). Subs., 0.3110· $Mg_2As_2O_7$, 0.1212
Calc. for $C_{14}H_{14}O_6N_3As$ N, 10 63, As, 18 98. Found N, 10.55; As, 18.81.

***N*-(Phenyl-4-arsonic Acid)-glycine-4′-aminoanilide,** *p*-$H_2O_3AsC_6H_4$-$NHCH_2CONHC_6H_4NH_2$(*p*-).—This substance could not be made directly from *p*-amino-chloroacetanilide because of the inaccessibility of the latter compound. It is also probable that the presence of the amino group would prevent a smooth reaction in the desired sense. The substance was therefore obtained indirectly, both by the saponification of the acetyl compound described below and by reduction[1] of the nitro compound just mentioned From the standpoint of yield the latter method is to be preferred. The former, however, is more rapid.

16 g. of (phenyl-4-arsonic acid)-glycine-4′-nitroanilide were dissolved in 50 cc. of hot 2 *N* sodium hydroxide solution, whereupon the sodium salt suddenly separated in finely divided form. This suspension was added to a bottle containing a slime of ferrous hydroxide prepared by precipitating a cold, saturated solution of 80 g. of ferrous sulfate with sufficient 25% sodium hydroxide solution to render the mixture strongly alkaline to litmus after thorough shaking. The reduction occurred at once in the cold, as evidenced by the change in color of the iron hydroxide. The bottle was immediately stoppered and shaken vigorously for several minutes and the mixture then poured on to a large suction funnel. On acidifying the filtrate with acetic acid a copious precipitate of the crude amino acid separated. This was filtered off, redissolved in hot, dil ammonia, and reprecipitated with acetic acid. For final purification it was dissolved in a considerable volume of warm, 10% sulfuric acid, treated with bone black, and sodium acetate solution added to the warm filtrate until it no longer turned congo red paper blue. The amino acid separated in almost quantitative yield as colorless, microscopic needles or platelets. When heated rapidly it decomposes at 253–4° with preliminary darkening. It is practically insoluble in boiling water or 50% alcohol and dissolves in dil. hydrochloric acid, the hydrochloride being readily salted out by an excess of the acid. The acid solution is readily diazotized, coupling with R-salt to form a red dye.

Subs., 0.1345 13 25 cc. N (24.5°, 760 mm.). Subs., 0.1553: $Mg_2As_2O_7$, 0.0654.
Calc. for $C_{14}H_{16}O_4N_3As$ N, 11.51; As, 20.52. Found N, 11.31; As, 20.32.

Owing to the comparative stability of the anilide linking in *N*-(phenyl-4-arsonic acid)-glycine-4′-acetamino-anilide (see below), it was possible to remove the acetyl group in this compound by short boiling with hydrochloric acid. A partial rupture of the anilide linking could not be avoided, however, and consequently a good yield of the amino compound was not obtained. The mechanical difficulties arising from the sparing solubilities of the hydrochlorides of both the acetamino and amino acids were overcome by the addition of alcohol to the hydrolysis mixture, and the following conditions were found to permit of a rapid and smooth reaction.

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[1] THIS JOURNAL, 40, 1580 (1918).

5 g. of *N*-(phenyl-4-arsonic acid)-glycine-4′-acetaminoanilide were suspended in a mixture of 45 cc. of 1 : 1 hydrochloric acid and 15 cc. of alcohol. On boiling the solution under a reflux condenser the arsonic acid gradually dissolved. After 10 minutes' boiling the clear solution was chilled, causing the precipitation of the hydrochloride of the aminoanilide. The mixture was diluted with water, treated with ammonia in slight excess, heated on the water bath, and acidified with acetic acid, the amino compound separating as minute microscopic needles agreeing in all properties with the substance obtained by the reduction of the nitro compound. The yield was 2 g.

Subs., 0 1539 15.6 cc N (22 0°, 760 mm) Subs , 0 2902 $Mg_2As_2O_7$, 0 1222

Calc. for $C_{14}H_{16}O_4N_3As$ N, 11 51, As, 20 52 Found N, 11 73, As, 20 30

N-(**Phenyl-4-arsonic Acid)-glycine-4′-acetaminoanilide.**—Owing to the sparing solubility of *p*-chloroacetylamino acetanilide[1] the reaction mixture remained a thick paste in this case After 4 hours' heating, however, the suspended material was changed in appearance and finally became completely soluble in dil. sodium hydroxide solution. The substance was purified in the usual manner. From hot, dilute solutions of the sodium salt acetic acid causes the gradual separation of the acid as aggregates of microscopic needles which are practically insoluble in boiling water or 50% alcohol and do not melt below 285°. 22 g. of arsanilic acid yielded 29 g. of the new arsonic acid.

Subs., 0.1459. 13.0 cc N (22.5°, 763 mm.).

Calc. for $C_{16}H_{18}O_5N_3As$. N, 10 32. Found 10 48

Sodium Salt.—On dissolving the arsonic acid in sodium hydroxide solution to a slight alkaline reaction and adding alcohol until crystallization begins, the salt gradually separates as minute, lustrous platelets which slowly lose part of their water of crystallization on exposure to the air. A portion recrystallized from hot water and air-dried also gave uncertain figures for water of crystallization.

Subs., air-dry, 0.4421. Loss, 0.0379 *in vacuo* at 100° over H_2SO_4

Calc. for $C_{16}H_{17}O_5N_3AsNa.2H_2O$: $2H_2O$, 7.75; $2^1/_2$ H_2O, 9.49. Found 8 57.

Subs., anhydrous, 0.1324: 11.4 cc. N (21.5°, 761 mm.). Subs., 0.3218. $Mg_2As_2O_7$, 0.1140.

Calc. for $C_{16}H_{17}O_5N_3AsNa$: N, 9 79; As, 17.47. Found: N, 9.99; As, 17.00.

N-(**Phenyl-4-arsonic Acid)-glycine-4′-uramino-anilide,** *p*-$H_2O_3AsC_6H_4$-

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[1] THIS JOURNAL, 39, 1455 (1917).

$NHCH_2CONHC_6H_4NHCONH_2$(*p′*-).—(From *p*-chloroacetylamino-phenyl urea.[1]) After one hour's boiling the arsonic acid suddenly separated from the clear solution. After an additional hour's heating the substance was filtered off and purified over the sodium salt described below. The free acid was precipitated by acetic acid from a hot solution of the salt as pale brown, microcrystalline aggregates which contain $^1/_2$ molecule of water of crystallization. It is very sparingly soluble in boiling water, 50% alcohol, or methyl alcohol. When rapidly heated the anhydrous substance darkens above 200° and decomposes at 230°.

Subs., air-dry, 1.1959 Loss, 0.0299 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{15}H_{17}O_5N_4As.0.5H_2O$ H_2O, 2.16 Found 2.50
Subs., anhydrous, 0.1555 19.0 cc N (27.0°, 759 mm.)
Calc. for $C_{15}H_{17}O_5N_4As$ N, 13.73 Found 13.89

Sodium Salt.—A neutral solution of the crude acid as obtained above in a small volume of dil. sodium hydroxide solution was treated with an equal volume of saturated sodium acetate solution. On standing in the refrigerator the salt crystallized as a thick mass of colorless microscopic needles. These were filtered off, washed with 85% alcohol, and recrystallized by dissolving in a small volume of warm water and treating the solution with an equal volume of alcohol. The filtered product was washed with 50% alcohol. Starting with 22 g. of arsanilic acid the yield was 24 g. The salt contains 4 molecules of water of crystallization.

Subs., air-dry, 0.5620 Loss, 0.0822 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{15}H_{16}O_5N_4AsNa.4H_2O$ H_2O, 14.35 Found 14.63.
Subs., anhydrous, 0.1311 14.8 cc N (20.5°, 756 mm.) Subs., 0.3050 $Mg_2As_2O_7$, 0.1087.
Calc. for $C_{15}H_{16}O_5N_4AsNa$ N, 13.02, As, 17.42. Found. N, 13.07; As, 17.20.

***N*-(Phenyl-4-arsonic Acid)-glycine-4′-methyl-5′-uramino-anilide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_3(CH_3)NHCONH_2$(*p′,m′*). — Starting with 18.4 g. of 2-methyl-5-chloroacetylamino-phenyl urea,[2] the crude acid which separated during the heating was dissolved in dil. sodium hydroxide solution, the filtrate diluted to about 500 cc., heated, and then acidified with acetic acid. The new arsonic acid separated as aggregates of microscopic platelets and hairs which rendered filtration difficult. The yield was 22 g. The substance contains approximately $^1/_2$ molecule of water of crystallization. When rapidly heated the anhydrous acid decomposes at 257–8° with preliminary darkening and sintering and is practically insoluble in the usual solvents.

Subs., air-dry, 0.5964 Loss, 0.0103 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{16}H_{19}O_5N_4As.0.5H_2O$: H_2O, 2.09. Found 1.73.
Subs., anhydrous, 0.1413 16.3 cc N (23.0°, 758 mm.). Subs., 0.3553: $Mg_2As_2O_7$, 0.1305
Calc. for $C_{16}H_{19}O_5N_4As$: N, 13.26; As, 17.76. Found. N, 13.27; As, 17.72.

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[1] THIS JOURNAL, 39, 1456 (1917).

[2] *Ibid.*, 39, 1464 (1917).

Sodium Salt.—A suspension of the acid in a little hot water was dissolved by adding just enough sodium hydroxide solution and treated with alcohol until just turbid. On rubbing and letting stand the salt slowly separated as a crystalline powder. A similar recrystallization was necessary to obtain an entirely pure product. The air-dried salt contained approximately 3.5 molecules of water of crystallization and was readily soluble in water. It can be recrystallized from hot water and is slowly salted out from strong solutions by sodium acetate.

Subs., air-dry, 0 7448 Loss, 0 0898 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{16}H_{18}O_5N_4AsNa$ 3 $5H_2O$· H_2O, 12.48. Found: 12 05

Subs., anhydrous, 0 1518 16 4 cc. N (21 5°, 768 mm.) Subs., 0.3272· $Mg_2As_2O_7$, 0 1174

Calc for $C_{16}H_{18}O_5N_4AsNa$ N, 12 61, As, 16 88 Found. N, 12 66, As, 17.31.

N-**(Phenyl-4-arsonic Acid)-glycine-3′-oxamylaminoaniline,** *p*-H_2O_3As-$C_6H_4NHCH_2CONHC_6H_4NHCOCONH_2$(*m*′-) —5 2 g. of *m*-chloroacetylamino-oxanilamide[1] were boiled 6 hours with the usual reaction mixture. The precipitate was then filtered off, suspended in about a liter of water and treated with a slight excess of ammonia. The insoluble material was collected by adding boneblack and the filtrate heated nearly to boiling. The addition of acetic acid caused the gradual deposition of the arsonic acid as slightly purplish, microcrystalline aggregates. The yield was 4.4 g. The acid is almost insoluble in boiling water and very sparingly soluble in boiling 50% alcohol. When rapidly heated it gradually darkens and partly decomposes, but does not melt up to 280°.

Subs, 0 1514 17 0 cc N (23.0°, 757 mm) Subs, 0 2985· $Mg_2As_2O_7$, 0 1076.

Calc. for $C_{16}H_{17}O_6N_4As$· N, 12 85, As, 17 19 Found N, 12 90, As, 17.39.

N-**(Phenyl-4-arsonic Acid)-glycine-4′-oxamylaminoanilide.**—Owing to the insolubility of *p*-chloroacetylamino-oxanilamide[2] the heating in this case was continued for about 7 hours, in spite of which the reaction was very incomplete. The filtered solid was susepnded in a large volume of water and the mixture treated with a slight excess of ammonia. After thorough disintegration of the insoluble residue the mixture was filtered and the solution acidified with acetic acid, causing the immediate precipitation of the arsonic acid as arborescent aggregates of microscopic needles. The yield from 4.8 g. of chloro compound was only 1.1 g. The substance is practically insoluble in all neutral solvents and does not melt below 280°.

Subs., 0.1812. 20.0 cc. N (20.5°, 755 mm). Subs., 0.2847. $Mg_2As_2O_7$, 0.1002.

Calc. for $C_{16}H_{17}O_6N_4As$· N, 12.85; As, 17.19. Found: N, 12.75; As, 16.99.

N-**(Phenyl-4-arsonic Acid)glycyl-2-aminophenol, (*N*-(Phenyl-4-arsonic Acid)-glycine-2′-hydroxyanilide),** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4$-OH(*o*-).—The halogen in the chloroacetylamino-phenols is extremely labile, so that these substances react with the amino group so readily as to render unnecessary the addition of sodium iodide as in the previously described syntheses. In the case of *o*-chloroacetylamino-phenol this reactivity causes a complication, since in the presence of alkalies or the sodium salts of weak acids it readily undergoes *ortho* condensation with the formation of *o*-amino-phenoxyacetic anhydride.[1] This reaction consequently paralleled the glycine formation, but in spite of this the desired arsonic acid was obtained, although in rather poor yield.

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[1] THIS JOURNAL, 39, 1452 (1917).

[2] *Ibid.*, 39, 1461 (1917).

4.4 g. of arsanilic acid were dissolved in 20 cc. of *N* sodium hydroxide solution and boiled under an air-condenser with 3.8 g. of *o*-chloroacetylamino-phenol[2] for one hour, the oil which first formed gradually disappearing. On cooling the reaction product separated as an oil, but on acidifying to congo red with hydrochloric acid and scratching, it solidified almost completely. The product was collected and digested with dil. ammonia, leaving 1.5 g. of a crystalline residue, which, both by melting point (170–5°) and analysis, was shown to be *o*-amino-phenoxyacetic anhydride. On warming the ammoniacal filtrate from this by-product and acidifying slightly with hydrochloric acid, 1 7 g. of the new arsonic acid separated on cooling as lustrous crystals. When rapidly heated the substance melts and decomposes at 190° with preliminary darkening. It is soluble in cold 95% alcohol and is also easily soluble in boiling water, from which it separates on cooling as long, narrow, glistening leaflets. An alkaline solution couples readily with diazotized sulfanilic acid, yielding an orange colored solution.

Subs., 0 1496· (Kjeldahl), 8.23 cc. 0.1 *N* HCl. Subs., 0.2221· $Mg_2As_2O_7$, 0.0958,
Calc. for $C_{14}H_{15}O_5N_2As$· N, 7.66; As, 20.48. Found: N, 7.70; As, 20.82.

A better yield of the arsonic acid was obtained by using two molecules of arsanilic acid instead of one molecule of sodium arsanilate. In this case longer boiling was necessary. 21 g. of *o*-chloroacetylamino-phenol and 50 g. of arsanilic acid (2 mols.) in 220 cc. of water were boiled under a reflux condenser for 4 hours. A clear solution was quickly obtained but this gradually darkened. At the end 50 cc. of 10% hydrochloric acid were added and on cooling and scratching the arsonic acid gradually crystallized. After purification as described above it agreed in all its properties with the product isolated by the first method. The yield was 17 g.

Subs., 0 1545: (Kjeldahl), 8.6 cc. 0.1 *N* HCl. Subs., 0.3010· $Mg_2As_2O_7$, 0.1254.
Calc. for $C_{14}H_{15}O_5N_2As$· N, 7.66; As, 20.48. Found: N, 7.76; As, 20.11.

***N*-(Phenyl-4-arsonic Acid)glycyl-3-aminophenol (*N*-(Phenyl-4-arsonic Acid)-glycine-*m*′-hydroxyanilide).**—Owing to the special importance of this substance as the starting material for the preparation of arseno-phenylglycine-bis-*m*′-hydroxyanilide, it will be published in connection with this arseno compound in another place.

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[1] Aschan, *Ber.*, 20, 1524 (1887).

[2] THIS JOURNAL, 41, 458 (1919).

N-**(Phenyl-4-arsonic Acid)-glycine-2′-methyl-5′-hydroxyanilide.**—When a solution of 12.4 g. of arsanilic acid in 57 cc. of *N* aqueous sodium hydroxide was boiled with 11.3 g. of 4-methyl-5-chloroacetylamino-phenol[1] a clear solution was obtained in a few minutes and deposition of the new arsonic acid began in about 20 minutes. Heating was continued on the water bath for a total of one hour, and after letting cool, the mixture was acidified to congo red with hydrochloric acid and filtered. The crude product was suspended in water, made just alkaline with sodium carbonate, and treated with boneblack after neutralizing with acetic acid. The filtrate, heated almost to the boiling point and treated with acetic acid, soon deposited the arsonic acid as glistening, pink platelets and microscopic prisms. The yield was 9.0 g., decomposing at about 220–5°, with preliminary darkening. It is very sparingly soluble in boiling water, alcohol, methyl alcohol, or acetic acid. In alkaline solution it couples with diazotized sulfanilic acid yielding a redder color than do similar compounds in which the position *para* to the hydroxy group is unoccupied.

Subs., 0.1308 (Kjeldahl), 7.0 cc. 0.1 *N* HCl. Subs., 0.3134: $Mg_2As_2O_7$, 0.1267.
Calc. for $C_{15}H_{17}O_5N_2As$: N, 7.37; As, 19.72. Found: N, 7.50; As, 19.49.

N-**(Phenyl-4-arsonic Acid)-glycine-4′-methyl-5′-hydroxyanilide.**—The product from 20 g. of 2-methyl-5-chloroacetylamino phenol[1] was worked up as in the case of the preceding compound, but as the analysis showed it to be impure it was converted into the sodium salt. The salt obtained by the addition of several volumes of alcohol to the neutral solution of the acid in sodium hydroxide solution was washed with 85% alcohol, and converted into the acid by precipitating from hot water with acetic acid. The arsonic acid forms prisms and branched leaflets which are very sparingly soluble in the usual solvents. The yield was 10.6 g. When rapidly heated to 255°, then slowly, the substance gradually darkens and softens, melting at 258° with decomposition. In alkaline solution it couples readily with diazotized sulfanilic acid.

Subs., 0.1596 (Kjeldahl), 12.1 cc. 0.1 *N* HCl. Subs., 0.3030: $Mg_2As_2O_7$, 0.1228.
Calc. for $C_{15}H_{17}O_5N_2As$: N, 7.37; As, 19.72. Found: N, 7.58; As, 19.57.

N-**(Phenyl-4-arsonic Acid)glycyl-4′-aminophenol,** (*N*-**(Phenyl-4-arsonic Acid)-glycine-4′-hydroxyanilide**).—After about 15 minutes the mixture (from 33 g. of arsanilic acid and 28 g. of *p*-chloroacetylamino-phenol[2]) set to an almost solid mass of lustrous crystals and the heating was continued for 45 minutes longer on the water bath. The somewhat colored product was suspended in a moderate volume of hot water and completely dissolved by the addition of dil. sodium hydroxide solution. After careful neutralization with acetic acid the hot solution was decolorized with bone-black and the clear, hot filtrate acidified with acetic acid, yielding the pure arsonic acid as faintly pink, glistening platelets in a yield of 35 g. When rapidly heated the arsonic acid darkens and melts to a black tar at 255–60°. It is almost insoluble in boiling water, 50% alcohol, 50% acetic acid, or methyl alcohol.

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[1] This Journal, 41, 459 (1919).

[2] *Ibid.*, 39, 1442 (1917).

Subs, 0 2673 (Kjeldahl), 14.25 cc 0.1 *N* HCl.
Calc. for $C_{14}H_{15}O_5N_2As$. N, 7.66. Found· 7.47

Sodium Salt.—This was readily obtained from a neutral solution of the acid in dil. sodium hydroxide on treatment with saturated sodium acetate solution. Recrystallized from hot water, the salt formed lustrous platelets which contained 4.5 molecules of water of crystallization. It is fairy easily soluble in cold water.

Subs, air-dry, 0.5730· Loss, 0 0967 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{14}H_{14}O_5N_2AsNa$ 4 $5H_2O$ H_2O, 17 26. Found 16 87.
Subs, anhydrous, 0 3096 (Kjeldahl), 16 25 cc. 0 1 *N* HCl; $Mg_2As_2O_7$, 0 1245
Calc for $C_{14}H_{14}O_5N_2AsNa$ N, 7 22, As, 19 30 Found N, 7 36, As, 19 41.

***N*-(Phenyl-4-arsonic Acid)-glycine-*p*′-anisidide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4OCH_3$(*p*-).—This substance was readily obtained by the usual method from chloroacetyl-*p*-anisidine in the presence of sodium iodide. The arsonic acid is precipitated by acetic acid from its hot solution in dil. sodium hydroxide as lustrous leaflets which darken and soften above 230° when rapidly heated. It is practically insoluble in boiling water or boiling 50% alcohol, and gives a flesh-colored solution in conc. sulfuric acid.

Subs., 0 1575 10.2 cc N (23 5°, 759 mm.) Subs., 0.3422 $Mg_2As_2O_7$, 0 1368.
Calc. for $C_{15}H_{17}O_5N_2As$· N, 7 37, As, 19 71. Found N, 7 45, As, 19.29.

***N*-(Phenyl-4-arsonic Acid)glycyl-1-amino-2-naphthol,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_{10}H_6OH$(1,2-).—The ease with which 1-chloroacetylamino-2-naphthol[1] reacts in the presence of alkali, alkali carbonates or salts of weak acids to form the anhydride of 1-amino-2-naphthoxyacetic acid interfered greatly with the preparation of the above arsonic acid, a fact which recalls the experience with *o*-chloroacetylamino-phenol. Of all the methods tested, the best results were given by the following procedure:

22 g. of arsanilic acid in 100 cc. of *N* sodium hydroxide solution, 20 g. of sodium iodide, 24 g. of chloroacetylamino-phenol and 100 cc. of alcohol were boiled for one hour, a large proportion of the chloroacetyl compound changing to the sparingly soluble anhydride. After dilution with water, the mixture was made ammoniacal and the insoluble anhydride (m. p. 215°) filtered off. The filtrate was acidified strongly with acetic acid and on standing in the refrigerator the arsonic acid gradually separated, contami-

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[1] This Journal, 41, 460 (1919).

nated with unchanged arsanilic acid. The deposited substance was redissolved in dil. ammonia, treated with boneblack, and the hot filtrate acidified with hydrochloric acid, the new compound separating at once as a heavy powder consisting of aggregates of microscopic plates and prisms which contained two molecules of water of crystallization. The yield was 6.5 g. The anhydrous substance decomposes at 189–91° with preliminary darkening and softening. Although very difficultly soluble in the cold it dissolves appreciably in boiling alcohol or acetic acid. It is more easily soluble in methyl alcohol and almost insoluble in water.

Subs., air-dry, 0.5668: Loss, 0.0453 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{18}H_{17}O_6N_2As.2H_2O$· H_2O, 7.96. Found: 7.99.

Subs., anhydrous, 0.1970· (Kjeldahl), 9.55 cc. 0.1 *N* HCl. Subs., 0.3666: $Mg_2As_2O_7$, 0.1386.

Calc. for $C_{18}H_{17}O_6N_2As$: N, 6.73; As, 18.02. Found: N, 6.79; As, 18.24.

(*N*-**(Phenyl-4-arsonic Acid)glycine-4′,1′-hydroxynaphthalide),** *N*-**(Phenyl-4-arsonic Acid)glycyl-4-amino-1-naphthol.**—4.4 g. of arsanilic acid were treated in the usual manner with 4.8 g. of 4-chloroacetylamino-1-naphthol[1] in 50% alcohol in the presence of sodium iodide for 4 hours. The deeply colored solution yielded the new arsonic acid on scratching and dilution with water. After filtration and washing with acetone in order to remove most of the color, the crude residue was dissolved in hot 20% sodium acetate solution and then treated with an equal volume of saturated sodium acetate solution. On cooling the sodium salt separated as glistening plates, and was recrystallized from a small volume of water. The yield was 4 g., containing 5.5 molecules of water of crystallization.

Subs., air-dry, 0.9469: Loss, 0.1704 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{18}H_{16}O_5N_2AsNa$ $5.5H_2O$. H_2O, 18.43. Found: H_2O, 17.99.

Subs., anhydrous, 0.2997. (Kjeldahl), 13.65 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1060.

Calc. for $C_{18}H_{16}O_5N_2AsNa$. N, 6.39; As, 17.11. Found: N, 6.38; As, 17.07.

On treating a hot, dilute solution of the sodium salt with acetic acid, the *free acid* separates slowly as microscopic crystals which contain approximately 1.5 molecules of water of crystallization. The anhydrous substance darkens above 200° and decomposes at 240–2°. It is practically insoluble in boiling water and but sparingly so in 50 or 95% alcohol. It is readily soluble in hot methyl alcohol.

Subs., air-dry, 0.6011: Loss, 0.0405 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{18}H_{17}O_5N_2As.1.5H_2O$: H_2O, 6.10. Found: 6.74.

Subs., anhydrous, 0.1452: 8.7 cc. N (27.5°, 760 mm.).

Calc. for $C_{18}H_{17}O_5N_2As$: N, 6.73. Found: 6.81.

N-**(Phenyl-4-arsonic Acid)glycyl-3-amino-4,6-dichlorophenol.**—In the reaction between 2,4-dichloro-5-chloroacetylamino-phenol[2] and sodium arsanilate by the usual sodium iodide-50% alcohol method a clear solution quickly formed from which the reaction product suddenly separated. The solid was suspended in a large volume of water to prevent separation of the somewhat difficultly soluble sodium salt and dil. sodium hydroxide solution added until all but an amorphous substance had dissolved. This was collected with boneblack and the filtrate heated and acidified with acetic acid. A repetition of this process removed a further small quantity of amorphous material, 26 g. of the original chloroacetyl compound yielding 21 g. of the pure product. The new arsonic acid forms flat, colorless microscopic needles which begin to darken above 220° but melt and decompose at about 280°. It is practically insoluble in boiling water or 50% alcohol.

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[1] This Journal, 41, 460 (1919).

[2] *Ibid.*, 41, 461 (1919).

Subs., 0.2538 (Kjeldahl), 12.02 cc 0.1 *N* HCl Subs., 0.2274 $Mg_2As_2O_7$, 0.0809
Calc. for $C_{14}H_{13}O_6N_2Cl_2As$ N, 6.44, As, 17.23 Found N, 6.64, As, 17.16

***N*-(Phenyl-4-arsonic Acid)glycyl-3-amino-6-bromophenol.**—16.5 g. of arsanilic acid and 20 g. of 2-bromo-5-chloroacetylamino-phenol[1] yielded smoothly 23 g. of recrystallized reaction product by the sodium iodide-50% alcohol method. Acetic acid precipitates the arsonic acid from hot solutions of its salts as glistening leaflets which decompose at 255° with preliminary sintering. It is very sparingly soluble in boiling water, 50% alcohol, or methyl alcohol.

Subs., 0.1421 7.6 cc N (21.5°, 763 mm.)
Calc for $C_{14}H_{14}O_6N_2BrAs$ N, 6.29 Found 6.23

***N*-(Phenyl-4-arsonic Acid)glycyl-4-amino-pyrocatechol, (*N*-(Phenyl-4-arsonic Acid)glycine-3′,4′-dihydroxyanilide).**—A solution of 33 g. of arsanilic acid in 150 cc. of *N* sodium hydroxide solution was boiled for one hour with 31 g. of 4-chloroacetylamino-pyrocatechol,[2] the reaction product partly separating from the deeply colored solution. After cooling the very dark crystalline mass was filtered off, dissolved in dil. sodium hydroxide solution and carefully neutralized with acetic acid. After treating the almost black solution with boneblack and acidifying the still deeply colored filtrate with acetic acid, the arsonic acid slowly separated as colored, microscopic leaflets. A repetition of the purification process removed most of the color, the product as finally obtained forming faintly pink, glistening leaflets. The yield was only 15 g., considerable loss having occurred during purification. When rapidly heated the substance blackens above 200° and decomposes at about 260–5°. It dissolves with difficulty in boiling water, separating on cooling as long, narrow, lustrous plates. It is very sparingly soluble in hot alcohol or methyl alcohol, more readily in hot 50% alcohol. A solution of the acid in an excess of dil. sodium hydroxide solution rapidly turns deep orange in color, while ferric chloride added to an aqueous solution of the acid causes a bluish purple coloration.

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[1] THIS JOURNAL, 41, 464 (1919).

[2] *Ibid.*, 41, 468 (1919).

Subs., 0.1653 (Kjeldahl), 8.67 cc. 0.1 *N* HCl Subs., 0.3105 $Mg_2As_2O_7$, 0.1274.
Calc. for $C_{14}H_{15}O_6N_2As$: N, 7.33; As, 19.61. Found: N, 7.34; As, 19.80.

***N*-(Phenyl-4-arsonic Acid)glycyl-anthranilic Acid,** p-$H_2O_3AsC_6H_4$-$NHCH_2CONHC_6H_4CO_2H$(*o*-).—Owing to the great reactivity of the chlorine atom in chloroacetyl-anthranilic acid the reaction between this compound and sodium arsanilic did not go entirely in the desired sense, so that the yield of the complex arsonic acid was unusually poor. The most satisfactory results were obtained by the use of the ester of chloroacetyl-anthranilic acid and subsequent saponification of the resulting ester arsonic acid.

30 g. of *N*-(phenyl-4-arsonic acid)glycyl-anthranilic ethyl ester (see below) were dissolved in a definite excess of 10% sodium hydroxide solution and allowed to stand at room temperature for several hours. Heating the solution was found not only to saponify the ester group but also to cleave the amide linking with consequent formation of anthranilic acid. Acidification caused the separation of a gum which rapidly crystallized and was redissolved in hot dil. sodium acetate solution and treated hot with an excess of hydrochloric acid. The arsonic acid separated at once as characteristic octahedra. The yield was 25 g. On rapid heating it decomposes at 230–5° with preliminary softening and darkening and is practically insoluble in boiling water, but appreciably in boiling methyl or ethyl alcohol or 50% alcohol.

Subs., 0.3056 (Kjeldahl), 15.4 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1195.
Calc. for $C_{15}H_{15}O_6N_2As$: N, 7.11; As, 19.02. Found: N, 7.06; As, 18.88.

***N*-(Phenyl-4-arsonic Acid)glycyl-anthranilic Ethyl Ester,** p-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4CO_2C_2H_5$(*o*-).—25 g. of chloroacetyl-anthranilic ethyl ester,[1] in the presence of sodium iodide yielded 31 g. of crude product. Recrystallized from 50% alcohol the ester separates as rosets of delicate needles which do not decompose below 280°. It is difficultly soluble in cold methyl alcohol, more readily on heating, and also dissolves in hot 50% or 95% alcohol.

Subs., 0.1485: 8.9 cc. N (25.5°, 755 mm.).
Calc. for $C_{17}H_{19}O_6N_2As$: N, 6.64. Found: 6.81.

***N*-(Phenyl-4-arsonic Acid)-glycyl-*N*-methylanthranilic Acid,** p-$H_2O_3AsC_6H_4NHCH_2CON(CH_3)C_6H_4CO_2H$(*o*-).—Although the reaction between sodium arsanilate and chloroacetyl-methylanthranilic acid[2] apparently proceeded partly in the desired sense, it was difficult to isolate a pure product. As in the case of the anthranilic acid compound the substance was found to be more easily prepared over the ester. For this purpose 25 g. of arsanilic acid dissolved in 115 cc. of *N* sodium hydroxide solution, 29 g. of chloroacetyl-methylanthranilic ethyl ester,[1] 22 g. of sodium iodide, and 115 cc. of alcohol were boiled under a reflux condenser for 4 hours. As attempts to obtain a crystalline reaction product failed the ester was not isolated. Instead the alcohol was allowed to boil off and the residue diluted with water After the oil which was formed had settled, the aqueous layer was decanted and the oil again shaken with a small volume of water which was then also decanted. The crude ester so obtained was dissolved in 150 cc. of 10% sodium hydroxide solution, filtered, and allowed to stand 4 hours at room temperature. The alkaline solution was then acidified to congo red with hydrochloric acid, causing the separation of the acid as a gum which gradually solidified. This was purified by again dissolving in dil alkali and acidifying with hydrochloric acid until faintly acid to congo red. The resulting cloudy solution gradually deposited the acid as microscopic aggregates of needles or short, flat plates. The yield was 16 g When rapidly heated the acid darkens and decomposes at 230°. It is very difficultly soluble in boiling water or boiling methyl alcohol, but fairly readily so in hot 50% alcohol, from which it can be recrystallized.

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[1] THIS JOURNAL, 41, 469 (1919).
[2] *Ibid.*, 41, 470 (1919).

Subs., 0.3213 (Kjeldahl), 15 7 cc 0 1 *N* HCl Subs , 0 3256 $Mg_2As_2O_7$, 0 1245
Calc for $C_{16}H_{17}O_6N_2As$. N, 6 86, As, 18.36. Found N, 6 85, As, 18 46

N-(Phenyl-4-arsonic Acid)glycyl-2-amino-benzamide, *p*-$H_2O_3AsC_6H_4$-$NHCH_2CONHC_6H_4CONH_2$(*o*-).—After boiling equivalent amounts of sodium arsanilate, *o*-chloroacetylamino-benzamide,[2] and sodium iodide for two hours in 50% alcohol a clear solution resulted. Crystallization of the reaction product was started by rubbing with a rod and the crude product purified by dissolving in dil. sodium hydroxide and adding acetic acid. In this way it crystallizes slowly as faintly yellow, radiating masses of delicate microscopic needles which contain one molecule of water of crystallization. When rapidly heated to 165° and then slowly it sinters and slowly melts down at 170°. It is sparingly soluble in cold water, alcohol or 50% alcohol, but readily soluble on warming. It is appreciably soluble in methyl alcohol in the cold.

Subs , air-dry, 0 8645. Loss, 0 0384 *in vacuo* at 100° over H_2SO_4
Calc for $C_{15}H_{16}O_5N_3As$ H_2O H_2O, 4 38 Found 4 44
Subs., anhydrous, 0 1828 (Kjeldahl), 14 05 cc 0 1 *N* HCl.
Calc. for $C_{15}H_{16}O_5N_3As$ N, 10 69 Found 10 76.

Sodium Salt.—The neutral solution of the acid in a small volume of dil. sodium hydroxide, was treated with several volumes of alcohol. On standing in the refrigerator the salt gradually crystallized. On recrystallization from 85% alcohol it formed globules of minute crystals which, like the acid, had a slightly yellow color. It contains 4.5 molecules of water of crystallization and dissolves readily in water.

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[1] THIS JOURNAL, 41, 470 (1918).

[2] *Ibid*, 39, 1442 (1917).

Subs., air-dry, 0.5076: Loss, 0 0808 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{15}H_{15}O_5N_3AsNa.4\ 5H_2O$: H_2O, 16.33. Found. 15.92.

Subs., anhydrous, 0.3235: (Kjeldahl), 23.65 cc. 0 1 *N* HCl. Subs., 0.3825: $Mg_2As_2O_7$, 0 1441.

Calc. for $C_{15}H_{15}O_5N_3AsNa$. N, 10 13; As, 18.06. Found· N, 10.24, As, 18.18.

N-**(Phenyl-4-arsonic Acid)glycyl-3-amino-benzamide.**—As in the previous case *m*-chloroacetylamino-benzamide[1] yielded after several hours' boiling a supersaturated solution of the reaction product which crystallized only on chilling and rubbing. On treating a solution of the crude product in dil. sodium hydroxide with acetic acid the pure arsonic acid separated as irregular, microscopic platelets. Recrystallized from hot 50% alcohol, in which it is rather sparingly soluble, it separates as rosets of microscopic spears which contain between 2 and 2.5 molecules of water of crystallization. The acid is practically insoluble in boiling water, and when rapidly heated, darkens and shows signs of decomposition above 200° but does not decompose completely until 280° is reached.

Subs., air-dry, 0.9688. Loss, 0 0891 *in vacuo* at 100° over P_2O_5

Calc. for $C_{15}H_{16}O_5N_3As.2H_2O$ H_2O, 8.39; 2.5 H_2O, 10.27. Found. 9 20.

Subs., anhydrous, 0.2713: (Kjeldahl), 20.5 cc 0.1 *N* HCl, $Mg_2As_2O_7$, 0.1075.

Calc for $C_{15}H_{16}O_5N_3As$. N, 10 69, As, 19 07 Found. N, 10 59; As, 19.13.

N-**(Phenyl-4-arsonic Acid)-glycyl-3-aminobenzoyl-urea,** *p*-$H_2O_3AsC_6H_4$-$NHCH_2CONHC_6H_4CONHCONH_2$(*m*-).—In this case the sparingly soluble *m*-chloroacetyl-aminobenzoyl-urea,[2] was gradually replaced by the new arsonic acid. After 4 hours' heating the resulting product was collected, suspended in water, and treated with dil. sodium carbonate solution until the solution remained slightly alkaline on thorough mixing and the arsonic acid was completely extracted from an insoluble residue. This was collected in the cold with boneblack and the clear filtrate treated with sodium acetate until the sodium salt separated. After standing in the refrigerator the salt was filtered off and washed with 20% sodium acetate solution, then with 85% alcohol. For purification it was dissolved in a small volume of water and treated with two volumes of alcohol. On scratching the sodium salt separated as thick, colorless masses of delicate microscopic hairs which contained 8 molecules of water of crystallization.

Subs , air-dry, 0 5560: Loss, 0.1323 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{16}H_{16}O_6N_4AsNa.8H_2O$. H_2O, 23.93. Found: 23.80.

Subs., anhydrous, 0.1335: 14.45 cc. N (26.0°, 756 mm.). Subs., 0.2892: $Mg_2As_2O_7$, 0.0970.

Calc. for $C_{16}H_{16}O_6N_4AsNa$: N, 12.23; As, 16.36. Found: N, 12.29; As, 16.19.

On addition of acetic acid to the hot dilute solution of the salt the free

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[1] THIS JOURNAL, 39, 1442 (1917).

[2] *Ibid.*, 39, 2430 (1917).

arsonic acid separates as sheaves and plumes of microscopic needles which decompose at about 280° with preliminary darkening and sintering. It is practically insoluble in boiling water or 50% alcohol.

Subs., 0.1663. (Kjeldahl), 15.25 cc. 0.1 *N* HCl.
Calc. for $C_{16}H_{17}O_6N_4As$: N, 12.84. Found: 12.84.

***N*-(Phenyl-4-arsonic Acid)glycyl-4-amino-benzamide.**—The reaction in the case of *p*-chloroacetylamino-benzamide[1] occurred quickly as evidenced by the rapid disappearance of the sparingly soluble chloroacetyl compound, followed soon after by the sudden precipitation of the new arsonic acid. This was suspended in water and dissolved by the careful addition of dil. sodium hydroxide solution. After neutralization to litmus with acetic acid the solution was heated, filtered, and the filtrate treated with sodium acetate until the sodium salt began to separate. This was recrystallized from hot water, in which it is easily soluble, separating on cooling as rosets of thin, microscopic needles which contain 4.5 molecules of water of crystallization.

Subs., air-dry, 0.3410: Loss, 0.0564 *in vacuo* at 100° over P_2O_5.
Calc. for $C_{15}H_{15}O_5N_3AsNa.4.5H_2O$: H_2O, 16.33. Found: 16.54.
Subs., anhydrous, 0.3187: (Kjeldahl), 22.5 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1210.
Calc. for $C_{15}H_{15}O_5N_3AsNa$: N, 10.13; As, 18.06. Found: N, 9.89; As, 18.33.

A hot, dilute solution of the salt, treated with acetic acid, immediately deposited the insoluble *arsonic acid* as nodules of microscopic needles which do not melt below 280°.

Subs., 0.1034: 9.7 cc. N (22.0°, 757 mm).
Calc. for $C_{15}H_{16}O_5N_3As$: N, 10.69. Found: N, 10.81.

***N*-(Phenyl-4-arsonic Acid)glycyl-5-amino-salicylamide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_3(OH)CONH_2$(*p,m*-).—42 g. of 5-chloroacetylamino-salicylamide,[2] by the sodium iodide method, after 2 hours boiling and purification of the crude product in the usual way, yielded 45 g. of the pure arsonic acid as glistening scales which contained one molecule of water of crystallization. When rapidly heated the anhydrous substance softens above 190° and gradually decomposes until fluid at about 255°. It is very sparingly soluble in boiling water or 50% alcohol, such solutions giving a brownish purple color with ferric chloride. In alkaline solution it couples with diazotized sulfanilic acid.

Subs., air-dry, 0.7932: Loss, 0.0356 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{15}H_{16}O_6N_3As.H_2O$: H_2O, 4.40. Found: H_2O, 4.49.
Subs., anhydrous, 0.3148 (Kjeldahl), 22.5 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1179.
Calc. for $C_{15}H_{16}O_6N_3As$: N, 10.27; As, 18.32. Found: N, 10.01; As, 18.08.

***N*-(Phenyl-4-arsonic Acid)-glycyl-3-amino-phenylacetamide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4CH_2CONH_2$(*m*-).—4.6 g. of *m*-chloroacetylamino-phenylacetamide,[1] using sodium iodide, gave a clear solution from which the crude product separated on dilution and rubbing. The substance was redissolved in dil. ammonia and treated with acetic acid, the pure arsonic acid separating as masses of microscopic needles which darken slightly above 220° and decompose at 275 80°. It is soluble in boiling water and 50% alcohol. The yield was 5.2 g.

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[1] This Journal, 39, 1443 (1917).

[2] *Ibid.*, 39, 2420 (1917).

Subs, 0 1427 12 8 cc N (22 0°, 764 mm) Subs., 0 3065 $Mg_2As_2O_7$, 0 1166.
Calc for $C_{10}H_{18}O_5N_2A$ N, 10 32, As, 18 41 Found N, 10 44, As, 18 35

N - **(Phenyl - 4 - arsonic Acid)glycyl - 4 - amino - phenylacetic Acid,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4CH_2CO_2H$(*p*-) —15.4 g. of arsanilic acid were dissolved in 70 cc. of *N* sodium hydroxide solution and boiled for one hour with 16 g of *p*-chloroacetylamino-phenylacetic acid.[2] The oil which separated on cooling soon crystallized and was triturated with 70 cc. of *N* hydrochloric acid solution, filtered off, washed with water, and dried. The yield of crude product, 24 g was dissolved in dil. sodium hydroxide solution, made faintly acid with acetic acid, treated with boneblack, and the filtrate diluted to about 500 cc., warmed on the water bath, and treated with hydrochloric acid until just acid to congo red. The arsonic acid which separated was recrystallized from 85% alcohol, separating slowly as practically colorless, microscopic globules. The dried acid gradually darkens on heating, finally melting and decomposing on keeping the bath at 280° for a few moments. The anhydrous substance is pale yellow, losing its color without dissolving when boiled with water. It is quite soluble in boiling 85% alcohol or methyl alcohol and dissolves only sparingly in boiling acetic acid.

Subs., 0 2077 (Kjeldahl), 10 25 cc 0 1 *N* HCl Subs, 0 2747 $Mg_2As_2O_7$, 0.1038.
Calc. for $C_{16}H_{17}O_6N_2As$ N, 6 87, As, 18 36. Found N, 6 91, As, 18.24.

N-**(Phenyl-4-arsonic Acid)glycyl-4-amino-phenylacetamide.** — (From *p*-chloroacetylamino-phenylacetamide[3] by the 50% alcohol and sodium iodide method). The crude acid was reprecipitated from its solution in hot dil. ammonia by acetic acid, separating as plumes of microscopic hairs. The arsonic acid is only sparingly soluble in boiling water or 50% alcohol and does not melt below 280°. Because of the aliphatic amide linking it is very sensitive to fixed alkali.

Subs, 0.1305 11.6 cc N (24 0°, 771 mm). Subs, 0 3092 $Mg_2As_2O_7$, 0 1192
Calc. for $C_{16}H_{18}O_5N_3As$: N, 10 32, As, 18 41 Found N, 10.3 ; As, 18.58.

Sodium Salt.—The acid was suspended in a small volume of water and very cautiously treated with dil. sodium hydroxide solution until just dissolved. The solution was then carefully neutralized to litmus with acetic acid and alcohol added until crystallization began. The salt

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[1] This Journal, **39**, 2421 (1917).

[2] *Ibid.*, **41**, 469 (1919).

[3] *Ibid.*, **39**, 1444 (1917)

separated as glistening platelets which, after air-drying, contained 2.5 molecules of water of crystallization and dissolved readily in water.

Subs., air-dry, 0.3945: Loss, 0.0371 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{16}H_{17}O_5N_3AsNa.2.5H_2O$ H_2O, 9.49. Found: 9.40.

Subs., anhydrous, 0.1489: 12.8 cc N (22.0°, 756 mm.). Subs., 0.2625: $Mg_2As_2O_7$, 0.0936.

Calc. for $C_{16}H_{17}O_5N_3AsNa$: N, 9.79, As, 17.47. Found: N, 9.91; As, 17.21.

***N*-(Phenyl-4-arsonic Acid)-glycyl-4-amino-phenylacetureide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4CH_2CONHCONH_2$(*p*-). — The very sparingly soluble *p*-chloroacetylamino-phenylacetylurea,[1] was very slowly and incompletely replaced by the reaction product. After 5 hours' boiling the somewhat gelatinous mass was diluted with water and filtered, and in order to extract the desired arsonic acid completely the residue was placed in a bottle with several hundred cc. of water containing a slight excess of ammonia and the mixture shaken in a machine until thoroughly disintegrated. Boneblack was then added and the mixture again shaken in order to collect the insoluble, gelatinous material. The filtrate was heated and acidified with acetic acid, causing the separation of the crystalline arsonic acid. This was converted into the *sodium salt* by suspending in a small volume of warm water and very cautiously treating with dil. sodium hydroxide until solution was just complete and the reaction was only faintly alkaline to litmus. The filtered solution was warmed and treated with alcohol until turbid, the salt separating on cooling as microscopic, hexagonal plates which contained 3 molecules of water of crystallization. The yield was 4.7 g.

Subs., air-dry, 0.4511: Loss, 0.0483 *in vacuo* at 100° over H_2SO_4

Calc. for $C_{17}H_{18}O_6N_4AsNa.3H_2O$: H_2O, 10.27. Found: 10.71.

Subs., anhydrous, 0.1500: 15.6 cc N (25.0°, 758 mm.). Subs., 0.2521: $Mg_2As_2O_7$, 0.0815.

Calc. for $C_{17}H_{18}O_6N_4AsNa$: N, 11.87; As, 15.88. Found: N, 11.88; As, 15.61.

On adding acetic acid to a hot solution of the sodium salt the free *arsonic acid* separated gradually as plumes of minute hairs which are almost insoluble in boiling water or 50% alcohol. It darkens slightly, but does not melt below 280°.

Subs., 0.1538: (Kjeldahl), 13.45 cc. 0.1 *N* HCl.

Calc for $C_{17}H_{19}O_6N_4As$: N, 12.45. Found: 12.25.

***N*-(Phenyl-4-arsonic Acid)-glycyl-2-amino-phenoxyacetamide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4OCH_2CONH_2$(*o*-).—The reaction product from *o*-chloroacetylamino-phenoxyacetamide,[2] was dissolved in dil. ammonia in order to avoid danger of saponification of the amide group. The addition of acetic acid to the heated filtrate caused the separation of the acid as a voluminous mass of microscopic needles which contained one molecule of water of crystallization. The yield was 10 g. The acid is very sparingly soluble in boiling water and somewhat more so in hot 50% alcohol, from which it crystallizes in minute, glistening needles on cooling. When anhydrous it decomposes at about 280° with preliminary darkening

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[1] This Journal, 39, 2434 (1917).

[2] *Ibid.*, 39, 2422 (1917).

Subs., air-dry, 0.0845 Loss, 0.0033 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{16}H_{18}O_6N_2As \cdot H_2O$: H_2O, 4.08 Found 3.90

Subs., anhydrous, 0.1370: 11.95 cc. N (23.0°, 756 mm.) Subs., 0.3369: $Mg_2As_2O_7$, 0.1222

Calc. for $C_{16}H_{18}O_6N_2As$: N, 9.93, As, 17.72 Found N, 10.02, As, 17.50

N-**(Phenyl-4-arsonic Acid)-glycyl-3-amino-phenoxyacetic Acid,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4OCH_2CO_2H$(*m*-).—In this case the addition of sodium iodide as a catalyzer was unnecessary. 22 g. of arsanilic acid were dissolved in 100 cc. of *N* sodium hydroxide solution, 25 g. of *m*-chloroacetylamino-phenoxyacetic acid[1] were added and the mixture boiled for one hour. An oil separated from the clear solution on cooling. On the addition of hydrochloric acid in excess the new arsonic acid rapidly crystallized. After filtration it was dissolved in sufficient dil. sodium hydroxide solution, diluted to about 500 cc. and warmed. On adding hydrochloric acid until congo red paper turned color, a finely divided, oily suspension was formed which solidified on rubbing, forming radiating masses of microcrystals containing approximately one molecule of water of crystallization. The yield was 28 g. The acid is fairly easily soluble in boiling water or 50% alcohol. When rapidly heated the anhydrous substance softens at 180–90°, then darkens and finally decomposes at about 250–60°.

Subs., air-dry, 0.5668 Loss, 0.0197 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{16}H_{17}O_7N_2As \cdot H_2O$: H_2O, 4.07 Found 3.47

Subs., anhydrous, 0.1583 (Kjeldahl), 7.53 cc. 0.1 *N* HCl Subs., 0.3019: $Mg_2As_2O_7$, 0.1088.

Calc. for $C_{16}H_{17}O_7N_2As$: N, 6.60, As, 17.68 Found N, 6.66, As, 17.40

N-**(Phenyl-4-arsonic Acid)glycyl-4-amino-phenoxyacetic Acid.**—This substance was obtained as in the case of the previously described *meta* isomer, from *p*-chloroacetylamino-phenoxyacetic acid.[2] After 30 minutes' boiling the clear solution suddenly set to a thick, crystalline mass, after which heating was continued 30 minutes longer on the water bath. The product was dissolved in sufficient sodium hydroxide solution, diluted to about 500 cc., heated on the water bath, and acidified to congo red with hydrochloric acid. The arsonic acid immediately separated as a colorless powder, which appeared as minute globules under the microscope. The yield was 30 g. When a hot, dilute solution of the salt (see below) is acidified with acetic acid the arsonic acid gradually separates as aggregates of flat, microscopic needles and platelets. It is practically insoluble in hot alcohol, methyl alcohol, or water, but is appreciably soluble in boiling 50% alcohol. The acid darkens above 250° but does not melt below 285°.

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[1] THIS JOURNAL, 41, 466 (1919).

[2] *Ibid.*, 39, 2436 (1917).

Subs., 0.1495: (Kjeldahl), 7.05 cc 0.1 *N* HCl.
Calc. for $C_{16}H_{17}O_7N_2As$: N, 6.61. Found, 6.59.

Sodium Salt.—On addition of alcohol to a neutral solution of the acid in dil. sodium hydroxide solution until crystallization started, the sodium salt separated as glistening, microscopic leaflets which contained 3 molecules of water of crystallization.

Subs., air-dry, 0.5258: Loss, 0.0535 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{16}H_{15}O_7N_2AsNa_2.3H_2O$: H_2O, 10.34. Found, 10.18.
Subs., anhydrous, 0.1441: 7.5 cc N (23.0°, 765 mm). Subs., 0.3417: $Mg_2As_2O_7$, 0.1133.
Calc. for $C_{16}H_{15}O_7N_2AsNa_2$: N, 5.99; As, 16.02. Found: N, 6.05; As, 16.02.

***N*-(Phenyl-4-arsonic Acid)-glycyl-4-amino-phenoxyacetamide.**—16 g. of *p*-chloroacetylamino-phenoxyacetamide[1] were employed, using sodium iodide. The reaction product which separated during the heating was purified by dissolving in dil. ammonia and reprecipitating with acetic acid. The yield was 16.5 g. The acid separates from hot, dilute solutions of its salts on adding acetic acid as sheaves and plumes of minute, flat needles which do not melt below 280°. It is very sparingly soluble in boiling water or 50% alcohol.

Subs., 0.1433: 12.6 cc N (22.0°, 747 mm).
Calc. for $C_{16}H_{18}O_6N_3As$: N, 9.93. Found: 10.01.

Sodium Salt.—As the amide group is rather sensitive to fixed alkali, sodium carbonate was used to dissolve the acid suspended in a small volume of hot water. The sodium salt began to separate on cooling and was more completely precipitated by adding sodium acetate solution. Recrystallized from water it formed long, flat, microscopic needles containing 5 molecules of water of crystallization.

Subs., air-dry, 1.3832: Loss, 0.2362 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{16}H_{17}O_6N_3AsNa.5H_2O$: H_2O, 16.83. Found: 17.08.
Subs., anhydrous, 0.2846 (Kjeldahl), 19.3 cc. 0.1 *N* HCl. Subs., 0.2936: $Mg_2As_2O_7$, 0.1010.
Calc. for $C_{16}H_{17}O_6N_3AsNa$: N, 9.44; As, 16.84. Found: N, 9.50; As, 16.60.

***N*-(Phenyl-4-arsonic Acid)glycyl-4-amino-phenoxyacetylurea,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4OCH_2CONHCONH_2$(*p*-). — 5.8 g. of the almost insoluble *p*-chloroacetylamino-phenoxyacetylurea[2] were gradually replaced by the new arsonic acid. After 4 hours the filtered product was suspended in warm water and sodium carbonate added until the arsonic acid was completely extracted from an insoluble residue and the solution remained just alkaline to litmus. The use of sodium hydroxide was avoided owing to the lability of the ureide group. The insoluble residue was collected with boneblack and the clear filtrate salted out with sodium acetate. After standing in the refrigerator the filtered salt was washed with 20% sodium acetate solution and then 85% alcohol, and purified by dissolving in a small volume of warm water and treating with two volumes of alcohol. On cooling the *sodium salt* gradually separated as aggregates of microscopic needles containing 4 molecules of water of crystallization. The yield was 4.5 g.

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[1] This Journal, 39, 2423 (1917).

[2] *Ibid.*, 39, 2435, 2436 (1917).

Subs., air-dry, 0.3254 Loss, 0.0419 *in vacuo* at 100° over H_2SO_4

Calc. for $C_{17}H_{18}O_7N_4AsNa\ 4H_2O$ H_2O, 12.86 Found 12.88

Subs., anhydrous, 0.1301 13.0 cc. N (25.0°, 766 mm.). Subs., 0.1479. $Mg_2As_2O_7$, 0.0467.

Calc for $C_{17}H_{18}O_7N_4AsNa$ N, 11.48, As, 15.36 Found N, 11.54; As, 15.24

On adding acetic acid to a hot, dilute solution of the salt the *arsonic acid* separated as rosets of microscopic needles which contained $^1/_2$ molecule of water of crystallization. The anhydrous acid slowly decomposes at about 290° with preliminary darkening, and is very difficultly soluble in boiling water or 50% alcohol.

Subs., air-dry, 0.4852. Loss, 0.0071 *in vacuo* at 100° over H_2SO_4

Calc. for $C_{17}H_{19}O_7N_4As\ 0.5H_2O$ H_2O, 1.89. Found 1.46.

Subs., anhydrous, 0.1580. (Kjeldahl), 13.45 cc 0.1 *N* HCl

Calc. for $C_{17}H_{19}O_7N_4As$ N, 12.02. Found. 11.92

***N*-(Phenyl-4-arsonic Acid)glycyl-3-methyl-4-amino-phenoxyacetic Acid,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_3(CH_3)OCH_2CO_2H$(*o,p*-).—4.4 g. of arsanilic acid, dissolved in 20 cc of *N* sodium hydroxide solution, and 5.2 g. of 3-methyl-4-chloroacetylamino-phenoxyacetic acid[1] yielded a clear solution on boiling. On chilling after one hour an oil separated and slowly crystallized. A solution of the crude substance in dil. sodium hydroxide was warmed and acidified with hydrochloric acid to congo red, after which the small amount of flocculent precipitate carrying coloring matter was rapidly filtered off. On cooling and standing 3 g. of the arsonic acid slowly separated as a crust on the sides of the vessel. For analysis it was recrystallized from a small volume of 50% alcohol. As so obtained the substance decomposes from 250–260° with preliminary sintering. The acid is difficult to obtain in well-defined crystals as it easily forms supersaturated solutions, crystallizes very slowly, and separates as a gum when rapidly thrown out of solution. When a dilute solution of the sodium salt described below is acidified with acetic acid the substance separates very gradually as warty aggregates of microscopic needles which decompose at 270° with preliminary darkening. It is appreciably soluble in methyl alcohol and in boiling water and readily in hot methyl or ethyl alcohol.

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[1] THIS JOURNAL, 39, 2201 (1917).

Subs., 0.2008: (Kjeldahl), 9.08 cc. 0.1 *N* HCl. Subs., 0.1802: $Mg_2As_2O_7$, 0.0660.
Calc. for $C_{17}H_{15}O_7N_2As$: N, 6.39; As, 17.12. Found: N, 6.33; As, 17.68.

Sodium Salt.—When a hot, neutral solution of the acid in a small volume of sodium hydroxide solution was treated with alcohol it yielded an oil which gradually crystallized on cooling and standing, while well-defined needles slowly separated from the supernatant liquor. The salt obtained in this way contained water of crystallization but the amount was not determined. It is easily soluble in water.

Subs., anhydrous, 0.3198: (Kjeldahl), 13.45 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1040.
Calc. for $C_{17}H_{13}O_7N_2AsNa_2$: N, 5.81, As, 15.54. Found. N, 5.89; As, 15.69.

***N*-(Phenyl-4-arsonic Acid)glycyl-3-amino-benzenesulfonamide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4SO_2NH_2$(*m*-).—Equivalent amounts of sodium arsanilate, *m*-chloroacetylamino-benzenesulfonamide,[1] and sodium iodide in 50% alcohol yielded a clear solution after several hours' boiling, from which the reaction product crystallized on cooling and rubbing. The collected product, after solution in dil. ammonia, was precipitated by acetic acid as *flat, glistening, microscopic needles, often grouped in* rosets. 21.5 g. of the chloroacetyl compound yielded 25 g. of the arsonic acid. It decomposes at about 265° with preliminary darkening and is difficultly soluble in boiling water or 50% alcohol.

Subs., 0.1755. 15 cc. N (23.0°, 756 mm.).
Calc. for $C_{14}H_{16}O_6N_3SAs$: N, 9.79. Found 9.81

***N*-(Phenyl-4-arsonic Acid)glycyl-4-amino-benzenesulfonic Acid,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4SO_3H$(*p*-).—16.5 g. of arsanilic acid were dissolved in 75 cc. of *N* sodium hydroxide solution and 25 g. of sodium chloroacetyl-sulfanilate[2] were added. After boiling the mixture for 30 minutes and cooling, the resulting clear solution was treated with an excess of hydrochloric acid. The arsonic acid separated on rubbing and was filtered off and washed with 10% hydrochloric acid. Reprecipitated from solution in dil. ammonia with hydrochloric acid, the pure arsonic acid separated slowly as flat, lustrous needles. The yield was 20 g. The acid is appreciably soluble in cold water, but less so in 10% hydrochloric acid solution. It is readily soluble in hot water, from which it separates on cooling as aggregates of minute, flat needles which contain two molecules of water of crystallization. It is sparingly soluble in alcohol and practically insoluble in acetone. The anhydrous substance slowly softens and decomposes at 245–6°.

Subs., air-dry, 0.8815: Loss, 0.0683 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{14}H_{15}O_7N_2SAs.2H_2O$: H_2O, 7.73. Found: 7.75.
Subs., anhydrous, 0.1537. (Kjeldahl), 7.14 cc. 0.1 *N* HCl. Subs., 0.3036: $Mg_2As_2O_7$, 0.1076.
Calc. for $C_{14}H_{15}O_7N_2SAs$: N, 6.51; As, 17.42. Found: N, 6.50; As, 17.11.

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[1] THIS JOURNAL, 39, 2429 (1917).

[2] *Ibid.*, 41, 470 (1919).

***N*-(Phenyl-4-arsonic Acid)glycyl-4-amino-benzenesulfonamide.**—The product from 21.5 g. of *p*-chloroacetylamino-benzenesulfonamide[1] in the presence of sodium iodide, was dissolved in dil. ammonia. On acidification of the hot, dilute solution with acetic acid the new arsonic acid rapidly separated as colorless aggregates of thin, microscopic leaflets and needles. The yield was 30 g. The acid is insoluble in boiling water or 50% alcohol, and on rapid heating sinters slightly, but does not melt below 280°.

Subs., 0.1374: 11.6 cc. N (20.0°, 769 mm.) Subs., 0.3019: $Mg_2As_2O_7$, 0.1078.
Calc. for $C_{14}H_{16}O_6N_3SAs$: N, 9.79; As, 17.45. Found: N, 9.95; As, 17.23.

***N*-(Phenyl-4-arsonic Acid)glycyl-4-amino-6-hydroxybenzenesulfonic Acid,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_3(OH)SO_3H$(*m*,*p*-).—22 g. of arsanilic acid in 100 cc. of *N* sodium hydroxide solution and 30 g. of the sodium salt of 4-chloroacetylamino-6-hydroxybenzenesulfonic acid[2] were boiled for 30 minutes and the clear solution then chilled and treated with 25 cc. of conc. hydrochloric acid. On scratching and standing in the refrigerator the reaction product crystallized and was filtered off and washed with 10% hydrochloric acid. The crude substance was suspended in water, treated with sodium acetate solution until completely dissolved, warmed, and the solution then treated with conc. hydrochloric acid until a concentration of about 10% hydrochloric acid was reached. On cooling the arsonic acid slowly separated as a thick crust of crystals which was washed with 10% hydrochloric acid and then with ice water. The yield was 25 g. The acid separates with approximately 1.5 molecules of water of crystallization and is fairly readily soluble in water at ordinary temperatures, but like many sulfonic acids it is less soluble in dil. hydrochloric acid. It separates from hot water on thorough chilling as microscopic leaflets and is difficultly soluble in hot alcohol, methyl alcohol or acetic acid. In alkaline solution it couples readily with diazotized sulfanilic acid. The anhydrous substance softens and darkens above 200°, but does not melt below 275°.

Subs., air-dry, 0.7833: Loss, 0.0488 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{14}H_{15}O_8N_2SAs.1.5H_2O$: H_2O, 5.71. Found: 6.23.
Subs., anhydrous, 0.2022 (Kjeldahl), 9.25 cc. 0.1 *N* HCl. Subs., 0.2258: $Mg_2As_2O_7$, 0.0798.
Calc. for $C_{14}H_{15}O_8N_2SAs$: N, 6.28; As, 16.81. Found: N, 6.40; As, 17.06.

***N*-(Phenyl-4-arsonic Acid)glycyl-4-amino-acetophenone,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4COCH_3$(*p*-).—4.3 g. of *p*-chloroacetylamino-acetophenone[3] with sodium iodide yielded 4 g. of the crystalline arsonic acid, after purification in the usual manner. The acid separates from hot, dilute solutions of its salts on addition of acetic acid as long, fine hairs which do not melt below 280°. It is almost insoluble in boiling water and but sparingly so in hot 50% alcohol. It dissolves in conc. sulfuric acid with a yellow color.

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[1] This Journal, 39, 2429 (1917).
[2] *Ibid.*, 41, 471 (1919).
[3] *Ibid.*, 41, 469 (1919).

Subs., 0.1538: 9.6 cc. N (25.5°, 768 mm.). Subs., 0.3164: $Mg_2As_2O_7$, 0.1240.

Calc. for $C_{16}H_{17}O_6N_2As$: N, 7.15; As, 19.10. Found: N, 7.22; As, 18.91.

(B) Derivatives of *o*-Arsanilic acid.

***N*-(Phenyl-2-arsonic Acid)glycineanilide** *o*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_5$.—This substance was prepared in the same way as the *p*-derivative from *o*-arsanilic acid[1] and chloroacetanilide. The arsonic acid separated slowly on standing, and precipitation was completed by diluting the reaction mixture. The crude product was ground up with dil. hydrochloric acid and recrystallized from 50% alcohol, crystallizing on seeding as radiating masses of minute prisms with one molecule of water of crystallization. The yield equaled the amount of *o*-arsanilic acid used. The anhydrous substance softens at 158°, melts at 160–3° with slow gas evolution, and dissolves very easily in boiling 50% alcohol, *although sparingly in the cold. It is very difficultly soluble in boiling* water and also in cold acetic acid, but dissolves readily in the latter on warming. It is also easily soluble in cold methyl alcohol, less readily in ethyl alcohol.

Subs., air-dry, 0.6579 Loss, 0.0363 *in vacuo* at 100° over H_2SO_4

Calc. for $C_{14}H_{15}O_4N_2As.H_2O$: H_2O, 4.89. Found. 5.52.

Subs., anhydrous, 0.2171: (Kjeldahl), 12.25 cc 0.1 *N* HCl. Subs., 0.3047: $Mg_2As_2O_7$, 0.1364.

Calc. for $C_{14}H_{15}O_4N_2As$: N, 8.00; As, 21.39. Found N, 7.91; As, 21.60.

***N*-(Phenyl-2-arsonic Acid)glycyl-2-aminophenol.**—22 g. of *o*-arsanilic acid and 19 g. of *o*-chloroacetylamino-phenol in 200 cc. of 0.5 *N* sodium hydroxide solution were boiled for 1/2 hour. On cooling the clear solution deposited an oil, part of which dissolved on rendering the mixture ammoniacal, leaving a copious residue of *o*-amino-phenoxyacetic anhydride.[2] On acidifying the filtrate with hydrochloric acid the oil which first separated was soon followed by crystals, and on standing in the ice-box the entire product crystallized. The crude substance was dissolved in dil. ammonia and the solution then acidified faintly with acetic acid and treated with boneblack. On adding hydrochloric acid carefully to the hot filtrate until just acid to congo red the arsonic acid separated as beautiful balls of glistening needles which soon filled the liquid. The yield was 8 g., containing 0.5 molecule of water of crystallization. When anhydrous it melts and decomposes at 151–3°. From hot water, in which it is but sparingly soluble, it separates on cooling as long, silky needles. It is fairly readily soluble in cold alcohol or methyl alcohol and easily so in hot 50% alcohol. An alkaline solution couples readily with diazotize sulfanilic acid.

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[1] THIS JOURNAL, 40, 1583 (1918).

[2] Cf. the *p*-arsonic acid, p. 1621.

Subs., air-dry, 0 7450· Loss, 0 0197 *in vacuo* at 100° over H_2SO_4

Calc. for $C_{14}H_{15}O_5N_2As.0\ 5H_2O$ H_2O, 2.40. Found 2.64.

Subs., anhydrous, 0.2520 (Kjeldahl), 14.0 cc. 0 1 *N* HCl Subs, 0 2734· $Mg_2As_2O_7$, 0.1178.

Calc. for $C_{14}H_{15}O_5N_2As$ N, 7 66; As, 20.48. Found N, 7 78, As, 20 79

N-**(Phenyl-2-arsonic Acid)glycyl-3-aminophenol.**—22 g. of *o*-arsanilic acid dissolved in 100 cc. of *N* sodium hydroxide solution and 19 g. of *m*-chloroacetylamino-phenol[1] were boiled for 30 minutes. On cooling a deep red oil separated, but on adding hydrochloric acid until acid to congo red, it crystallized on rubbing. The substance was then filtered off, washed with water, suspended in a small volume of water, and dissolved by the addition of ammonia On rendering slightly acid with acetic acid the deep colored solution deposited a dark, gummy precipitate which was collected in the cold with boneblack and filtered. The filtrate was then heated with boneblack, which removed most of the color. A pink color still persisted in the filtrate, a property which all of the substances derived from *m*-chloroacetylamino-phenol have shown. The filtrate was diluted to about 500 cc., heated, and then treated with hydrochloric acid until congo red turned color, causing the momentary separation of an oil which on stirring rapidly crystallized, forming bundles of pink microscopic platelets which when air-dried contained approximately two molecules of water of crystallization and melted at 103–5°. The yield was 17 g. When anhydrous the substance softens at about 125–30° and melts completely with decomposition at about 180°. It is readily soluble in alcohol, methyl alcohol, acetic acid and hot water, and in alkaline solution couples readily with diazotized sulfanilic acid.

Subs., air-dry, 0.6155. Loss, 0.0590 *in vacuo* at 100° over H_2SO_4

Calc. for $C_{14}H_{15}O_5N_2As\ 2H_2O$ H_2O, 8 96. Found· 9 59.

Subs., anhydrous, 0.2355: (Kjeldahl), 12.55 cc. 0.1 *N* HCl. Subs., 0.3123: $Mg_2As_2O_7$, 0.1362.

Calc. for $C_{14}H_{15}O_5N_2As$: N, 7 66; As, 20.48. Found. N, 7.46, As, 21.04.

N-**(Phenyl-2-arsonic Acid)glycyl-4-aminophenol.**—Equimolecular quantities of *o*-arsanilic acid and *p*-chloroacetylamino-phenol yielded a dark colored solution from which an oil separated on cooling. This slowly solidified, especially after making definitely acid to congo red with hydrochloric acid. After standing in the ice-box the product was filtered off, washed, dissolved in dil. ammonia and the solution faintly acidified with acetic acid and treated with boneblack. On acidifying the hot filtrate to congo red with hydrochloric acid the arsonic acid again separated as an oil which soon crystallized. This substance was again dissolved in dil. ammonia and the solution acidified with acetic acid and again treated with boneblack to remove the color which still persisted. On diluting the filtrate to about 300 cc., heating, and adding hydrochloric acid until congo red paper just turned and as long as the oily emulsion which momentarily formed redissolved, the arsonic acid separated on scratching as a heavy powder, consisting of short, colorless, microscopic platelets. The filtered substance was washed with water. The yield was 16 g. from 22 g. of *o*-arsanilic acid. When rapidly heated the acid darkens and then melts and decomposes at 208–9°. It is very sparingly soluble in boiling water and easily in boiling methyl alcohol or 50% alcohol.

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[1] This Journal, 39, 1442 (1917).

Subs., 0.2331: (Kjeldahl), 12.9 cc. 0.1 *N* HCl. Subs., 0.2950: $Mg_2As_2O_7$, 0.1255.
Calc. for $C_{14}H_{15}O_5N_2As$: N, 7 66; As, 20.48 Found: N, 7.75; As, 20.53.

(C) Derivatives of *m*-Arsanilic Acid.

N-**(Phenyl-3-arsonic Acid)glycineanilide.**—(From *m*-arsanilic acid[1] and chloroacetanilide). On diluting the reaction mixture with water and rendering acid to congo red with hydrochloric acid the crystalline arsonic acid was gradually deposited. This was recrystallized first from 50% alcohol and finally from glacial acetic acid, separating from the latter as rosets of minute, cream-colored prisms which apparently contained solvent of crystallization. When rapidly heated to 215° and then slowly the dried substance darkens, then softens, and finally decomposes at 217–18°. It is rather sparingly soluble in hot water, but dissolves readily in hot 50% alcohol or acetic acid and is appreciably soluble in cold 95% alcohol.

Subs., 0.2422: (Kjeldahl), 14 25 cc. 0 1 *N* HCl. Subs., 0.2857: $Mg_2As_2O_7$, 0.1267.
Calc. for $C_{14}H_{15}O_4N_2As$: N, 8.00; As, 21.39. Found. N, 8 24; As, 21.40.

N-**(Phenyl-3-arsonic Acid)glycyl-2-aminophenol.**—Although the reaction between *m*-arsanilic acid and *o*-chloroacetylamino-phenol was accompanied by the formation of *o*-amino-phenoxyacetic anhydride, as in the case of *p*- and *o*-arsanilic acids, the amount of anhydride was much less than that formed when the isomeric acids were used. Consequently the yield of the complex arsonic acid was much greater than in the case of the *o*- or *p*-arsanilic acid.

The reaction mixture from 22 g. of *m*-arsanilic acid and 19 g. of *o*-chloroacetylamino-phenol yielded an oil on cooling which redissolved on rendering the mixture ammoniacal, leaving about 3 g. of *o*-aminophenoxyacetic anhydride. The filtrate was acidified to congo red with hydrochloric acid, causing the deposition of a viscous oil which slowly crystallized on rubbing and letting stand. After standing for 24 hours in the refrigerator the crude substance was filtered off and washed with water. The deep colored solution of this product in dil. ammonia was neutralized with acetic acid and treated with boneblack. The still colored filtrate was diluted to about 300 cc., heated on the water bath, and then treated with hydrochloric acid until congo red turned color. On scratching and keeping sufficiently warm the substance slowly crystallized as almost colorless, flat, microscopic needles. If allowed to chill it separated first as an oil carrying coloring matter with it. If properly heated and with constant manipulation with a rod crystallization was almost complete in about 15 minutes.

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[1] This Journal, 40, 1583 (1918).

After cooling it was filtered off and washed with water. The yield was 21 g. When rapidly heated to 185°, then slowly, the arsonic acid darkens and softens, finally melting and decomposing at 190–2°. It is sparingly soluble in cold water, more easily on boiling, and on cooling it again separates very slowly and incompletely. It is somewhat soluble in the cold in 50% or 95% alcohol, more easily on warming, and also dissolves in cold methyl alcohol or boiling acetic acid. A solution of the acid in strong ammonium acetate solution slowly deposits the ammonium salt as minute needles. Although hydrochloric acid precipitates the acid fairly completely from its salts as a gummy mass, an excess of acetic acid causes no immediate precipitate. However, on long standing the free arsonic acid separates slowly and incompletely from such solutions as a crust of broad, microscopic needles.

Subs., 0.1835. (Kjeldahl), 10.35 cc 0.1 *N* HCl. Subs., 0.3004: $Mg_2As_2O_7$, 0.1282.

Calc. for $C_{14}H_{15}O_4N_2As$: N, 7.66; As, 20.48. Found: N, 7.90; As, 20.57.

N-(**Phenyl-3-arsonic Acid)glycyl-3-aminophenol.**—26.4 g. of *m*-arsanilic acid and 23 g. of *m*-chloroacetylamino-phenol yielded a purple oil which slowly crystallized on scratching. Attempts at purifying this substance by the usual method of reprecipitating the acid from its solution in dil. alkali by either acetic or hydrochloric acid were unsuccessful since the compound easily formed supersaturated solutions from which it separated extremely slowly, usually as highly colored, amorphous flocks. The substance was best purified by dissolving in hot 50% acetic acid and treating with boneblack, most of the purple color still persisting in the filtrate. On standing in the refrigerator the acid gradually separated as a thick crust of crystals which carried down the color with them. The yield was 27.5 g. A futher recrystallization was then attempted from 50% alcohol, the solution depositing the substance slowly as a light purple powder consisting of minute, irregular platelets and flat needles containing approximately 1.5 molecules of water of crystallization. When rapidly heated to 150° the anhydrous substance gradually sinters to a tar which decomposes at about 180–90°. In the cold it is more soluble in methyl alcohol than in the other solvents, but is fairly easily soluble in hot water, more so in hot alcohol, acetic acid or in these solvents when diluted. It is practically insoluble in acetone, benzene or ether.

Subs., air-dry, 0.3468: Loss, 0.0210 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{14}H_{15}O_5N_2As.1.5H_2O$: H_2O, 6.87. Found: 6.06.

Subs., anhydrous, 0.1607: (Kjeldahl), 8.95 cc. 0.1 *N* HCl. Subs., 0.2531: $Mg_2As_2O_7$, 0.1058.

Calc. for $C_{14}H_{15}O_5N_2As$ N, 7.66; As, 20.48. Found: N, 7.80; As, 20.18.

***N*-(Phenyl-3-arsonic Acid)glycyl-4-aminophenol.**—The almost colorless oil obtained from 22 g. of *m*-arsanilic acid and 19 g. of *p*-chloroacetylamino-phenol could not be made to crystallize directly and was therefore dissolved by adding an equal volume of conc. hydrochloric acid to the reaction mixture, with chilling. On scratching, the clear solution deposited the hydrochloride of the arsonic acid as minute needles, the mixture setting to a thick mass after several hours. After filtering off, the hydrochloride was washed with 1 : 1 hydrochloric acid and was then suspended in water and dissolved by the addition of ammonia. The warm solution was treated with hydrochloric acid until acid to congo red, causing the partial separation of the substance as an oil which gradually crystallized on scratching. After standing in the refrigerator it was filtered off and washed with ice water. The yield was 21 g. When recrystallized from a small volume of hot water, in which it readily dissolves, it separates on rapid chilling as a milky emulsion which then very slowly crystallizes, partly as a hydrate. But if allowed to cool very slowly it separates gradually as microscopic platelets which are anhydrous. When rapidly heated the arsonic acid starts to sinter and darken above 170° and when held at 180° slowly shrinks together and decomposes. It is sparingly soluble in cold water but dissolves readily in the boiling solvent. It is easily soluble in hot alcohol, appreciably so in cold methyl alcohol, and but sparingly soluble in hot acetone. It dissolves in warm, dil. hydrochloric acid and on addition of the stronger acid it is converted into the hydrochloride, which separates slowly on rubbing.

Subs., 0.1527: (Kjeldahl), 8.47 cc. 0.1 *N* HCl. Subs., 0.3042: $Mg_2As_2O_7$, 0.1308.

Calc. for $C_{14}H_{15}O_5N_2As$: N, 7.66; As, 20.48. Found: N, 7.77; As, 20.75.

(D) Derivatives of Substituted *p*-Arsanilic Acids.

***N*-(2-Methylphenyl-4-arsonic Acid)glycyl-3-aminophenol.**—30 g. of the sodium salt of *o*-methylarsanilic acid (from *o*-toluidine) and 17 g. of *m*-chloroacetylamino-phenol, yielded an oil which rapidly crystallized on acidifying the mixture to congo red with hydrochloric acid. After dissolving the product in dil. ammonia and acidifying the solution with acetic acid, 17 g. of the pure arsonic acid separated as long, flat, microscopic needles. When heated to 285° the acid darkens and slowly decomposes. It is practically insoluble in boiling water, but is appreciably dissolved by hot 50% alcohol. An alkaline solution couples readily with diazotized sulfanilic acid.

Subs., 0.1338: 8.6 cc. N (28.5°, 763 mm.). Subs., 0.2924: $Mg_2As_2O_7$, 0.1182.

Calc. for $C_{15}H_{17}O_5N_2As$: N, 7.37; As, 19.72. Found: N, 7.31; As, 19.50.

***N*-(2-Methylphenyl-4-arsonic Acid)glycyl-4-aminophenol.**—This substance was obtained exactly as in the case of its isomer and in about the same yield. On acidifying a hot solution of the arsonic acid in dil. ammonia with acetic acid the free acid separates as microscopic, spindle-shaped needles. When rapidly heated it decomposes at 232–3° with preliminary darkening. It is very sparingly soluble in boiling water and slightly more soluble in hot 50% alcohol.

Subs., 0.1313: 8.6 cc. N (28.0°, 761 mm.). Subs., 0.3246: $Mg_2As_2O_7$, 0.1347.
Calc for $C_{15}H_{17}O_5N_2As$: N, 7.37; As, 19.72. Found: N, 7.44; As, 20.01.

N-**(3-Methylphenyl-4-arsonic Acid)glycyl-3-aminophenol.**—This substance was obtained as in the case of the two previously described compounds, starting with 2-methyl-4-amino-phenylarsonic acid.[1] Acetic acid slowly precipitates the compound from hot ammoniacal solution as aggregates of spindle-shaped micro-crystals. When rapidly heated it decomposes at 232–5° with preliminary softening and darkening. It is very sparingly soluble in boiling water or alcohol, more readily in hot 50% alcohol. An alkaline solution couples readily with diazotized sulfanilic acid.

Subs., 0.1682: 10.6 cc. N (21.0°, 755 mm.). Subs., 0.3100: $Mg_2As_2O_7$, 0.1275.
Calc for $C_{15}H_{17}O_5N_2As$: N, 7.37; As, 19.72. Found: N, 7.28; As, 19.84.

N-**(2-Carboxyphenyl-4-arsonic Acid)glycyl-3-aminophenol,** *o,p*-$HO_2C(H_2O_3As)C_6H_3NHCH_2CONHC_6H_4OH$(*m*-).—10 g. of 3-carboxy-4-amino-phenylarsonic acid,[2] were dissolved in 80 cc. of *N* sodium hydroxide solution (about 2 mols), then treated with 20 cc. of 2 *N* acetic acid and 8 g. of *m*-chloroacetylamino-phenol, and the mixture boiled for one hour. The reaction was apparently facilitated by the presence of the sodium acetate as buffer, since without the addition of acetic acid the solution would have reacted alkaline and decomposed the chloroacetylamino-phenol. On acidifying the clear, chilled solution with hydrochloric acid the reaction product crystallized. This was purified by redissolving in dil. sodium hydroxide, rendering faintly acid with acetic acid and adding boneblack in the cold to collect a small amount of flocculent material. The filtrate was warmed and then treated with an excess of acetic acid, the arsonic acid separating on scratching as thin, minute platelets. After washing with water and air-drying, the yield was 6 g. The acid separates with one molecule of water of crystallization and is practically insoluble in boiling water. It is somewhat soluble in hot alcohol or 50% alcohol and dissolves fairly readily in boiling methyl alcohol or glacial acetic acid. When rapidly heated the anhydrous substance darkens and swells, then decomposes at 204–7°. An alkaline solution couples readily with diazotized sulfanilic acid.

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[1] THIS JOURNAL, 40, 1588 (1918).

[2] Kahn and Benda, *Ber.*, 41, 3862 (1908).

Subs., air-dry, 0.5776: Loss, 0.0236 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{16}H_{15}O_7N_2As.H_2O$: H_2O, 4.21. Found: 4.09.

Subs., anhydrous, 0.1441: (Kjeldahl), 7.1 cc. 0.1 *N* HCl. Subs., 0.3292: $Mg_2As_2O_7$, 0.1231.

Calc. for $C_{16}H_{15}O_7N_2As$. N, 6.83; As, 18.28. Found. N, 6.90; As, 18.03.

NEW YORK, N. Y.

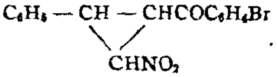
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY.]

STUDIES IN THE CYCLOPROPANE SERIES. VIII. NITRO-CYCLOPROPANE DERIVATIVES.

BY E. P. KOHLER AND H. E. WILLIAMS.

Received June 27, 1919.

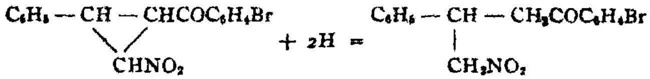
In continuation of the work reported in the preceding paper of this series,[1] we have studied another nitro-cyclopropane derivative in the hope that a substance which would give more sparingly soluble products would enable us to isolate some of the intermediate compounds that baffled us in the earlier work. We selected for the purpose *p*-bromo-benzoyl-phenyl-nitro-cyclopropane,



$$C_6H_5-CH-CHCOC_6H_4Br \;\; (\text{ring closed by } CHNO_2)$$

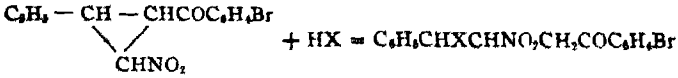
This nitro compound was made without much trouble by the method which had been developed for the bromine-free analog. It has 3 dissimilar asymmetric carbon atoms and 3 of the 4 possible stereoisomers were isolated in the course of the investigation. The structure of all of these is established by the fact that with various reagents they give products in which the carbon chain is not the same, showing that they are formed by opening a cyclopropane ring at different points.

On cautious reduction with zinc and alcohol all of the isomeric cyclopropane derivatives give the same substance that is obtained by addition of nitromethane to benzal-aceto-*p*-bromophenone. The ring is, therefore, opened between the carbon atoms holding the nitro- and *p*-bromobenzoyl groups:



$$\underset{CHNO_2}{C_6H_5-CH-CHCOC_6H_4Br} + 2H = \underset{CH_2NO_2}{C_6H_5-CH-CH_2COC_6H_4Br}$$

The isomeric cyclopropane derivatives also combine very readily with the halogen acids but the ring is opened at a different point:



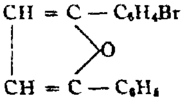
$$\underset{CHNO_2}{C_6H_5-CH-CHCOC_6H_4Br} + HX = C_6H_5CHXCHNO_2CH_2COC_6H_4Br$$

The reactions of the resulting halogen nitro compounds leave no doubt as to their structure. Thus the chlorine compound, when treated with cold potassium acetate, loses nitrous acid and forms an unsaturated chlorine compound, which gives benzoyl chloride on oxidation with ozone:

$$C_6H_5CHClCHNO_2CH_2COC_6H_4Br - HNO_2 = C_6H_5CCl = CHCH_2COC_6H_4Br$$

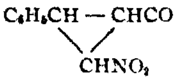
$$C_6H_5CCl = CHCH_2COC_6H_4Br \longrightarrow C_6H_5COCl + BrC_6H_4CO_2H + H_2O + 2CO_2$$

The more sensitive bromine compound loses hydrobromic acid more easily than nitrous acid, therefore forms an unsaturated nitro compound which gives benzaldehyde when oxidized. When boiled with alcohol alone it loses nitrous as well as hydrobromic acid. The result is a furane derivative,

$C_6H_5CHBrCHNO_2CH_2COC_6H_4Br =$  $+ HBr + HNO_2$

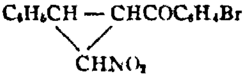
It is worthy of note that while these halogen nitro compounds have reactive hydrogen and halogen in the 1,3-relation they invariably give ethylene and not cyclopropane derivatives when halogen acid is eliminated.

The isomeric cyclopropane derivatives are also attacked by bromine. The principal product is an α,γ-dibromo compound,

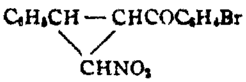
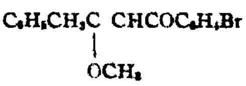
 $+ Br_2 = C_6H_5CHBrCHNO_2CHBrCOC_6H_5$

It is possible that this substance may be due to substitution of bromine in the α-position and addition of the resulting hydrogen bromide to the bromo cyclopropane thus formed, but no trace of such a bromo compound could be found among the products

The reaction of the cyclopropane derivatives which it is most difficult to interpret is that which takes place with alkalies. The final product, like that of the same reaction with the bromine free analog, is a β-diketone,

 $+ NaOH = NaNO_2 + C_6H_5CH_2COCH_2COC_6H_4Br.$

This diketone is manifestly formed as a result of a number of successive reactions. By using concentrated sodium methylate we succeeded in isolating an unsaturated methoxyl compound which readily gives the diketone on hydrolysis,

 $+ NaOCH_3 =$  $+ NaNO_2$

$$C_6H_5CH_2\underset{\substack{|\\ OCH_3}}{C}\ CHCOC_6H_4Br$$

It is possible that this is an intermediate product; but it seems more probable that both the methoxyl compound and the diketone are formed from an intermediate acetylenic ketone. In order to reach a definite conclusion, it will be necessary to find a method for detecting an acetylenic ketone in solutions.

Experimental Part.

γ-Nitro-β-phenyl-propyl-(4-bromophenyl) Ketone, $CH_2(NO_2)CH(C_6H_5)CH_2COC_6H_4Br$.—The saturated nitro-ketone that served as the starting point in the investigation was made by adding sodium nitromethane to *α*-phenyl-*γ*-(4-bromophenyl) propenone and acidifying the product. This reaction always gives two substances, one of which corresponds to the condensation of a molecule of nitro compound with one, the other with two molecules of the unsaturated ketone. In as much as the sodium compound formed by the addition of sodium nitromethane to the unsaturated ketone is more soluble than either sodium nitromethane or the unsaturated ketone, it is impossible to prevent the formation of considerable quantities of the "dimolecular" product. The following procedure gave the most satisfactory yield of the monomolecular compound.

A finely divided suspension of sodium nitromethane was made by adding 15 g. of nitromethane to a solution of 5 g. of sodium in 75 cc. of 95% alcohol and shaking vigorously until all lumps were broken up. The suspension was added rapidly to 58 g. of unsaturated ketone suspended in 150 g. of alcohol previously warmed to 60°. The mixture warmed up on shaking and the solid gradually disappeared. The resulting yellow to orange colored solution was immediately cooled in ice water and acidified with glacial acetic acid. By adding the acid drop by drop and stirring vigorously it was possible to get a coarsely crystalline product which was easily purified by thorough washing with water and alcohol and recrystallization from alcohol and benzene. The yield of pure substance was 87%.

The yield was not improved by using absolute methyl or ethyl alcohol. It fell to below 50% when the condensation was carried out in solution, or when the sodium nitromethane was added gradually, the principal product being the dimolecular compound. The yield is also less when the solution of sodium salt is acidified rapidly because a mixture of mono- and dimolecular products is precipitated as an oil. This later solidifies but the losses during purification are greater.

The nitro ketone crystallizes in small needles and melts at 101–2°. It is not very soluble in ligroin and alcohol, but dissolves readily in ether, chloroform, acetone and benzene.

Calc. for $C_{16}H_{14}O_3NBr$: Br, 23.0. Found: Br, 23.3, 23.0.

The semicarbazone of the nitro ketone is sparingly soluble in alcohol, moderately in acetone and in benzene. It melts with decomposition at 168–9°.

Calc. for $C_{17}H_{17}O_3N_4Br$: C, 51.5; H, 4.1. Found: C, 51.2; H, 4.2.

The "dimolecular" product, $CHNO_2(CH(C_6H_5)CH_2COC_6H_4Br)_2$, crystallized from benzene in fine needles. It is sparingly soluble in alcohol, more readily in ether, acetone, chloroform, and benzene.

Calc. for $C_{31}H_{25}O_4NBr_2$: C, 57.3; H, 3.9. Found: C, 57.5; H, 4.2.

γ - Nitro - β - phenyl - α - bromopropyl-(4-bromophenyl) Ketone, $CH_2(NO_2)CH(C_6H_5)CHBrCOC_6H_4Br$.—The nitro ketone was brominated in the usual way in carbon tetrachloride. The solution on evaporation under diminished pressure left a pale yellow oil which slowly solidified when allowed to stand in a cool place in contact with absolute methyl alcohol. The solid was washed with cold methyl alcohol and recrystallized from ordinary alcohol. It was thus separated into 4 substances—3 isomeric monobromo derivatives and one dibromo compound.

The principal product was a monobromo derivative which melted at 114.5–115.5°. This was most easily purified by crystallization from alcohol containing a small quantity of benzene. It separated in fine needles moderately soluble in alcohol, readily in benzene, acetone, and chloroform.

Calc. for $C_{16}H_{13}O_3NBr_2$: C, 45.0; H, 3.0. Found: C, 45.1; H, 3.4.

The mother liquors slowly deposited clear rhombic tables mixed with a small quantity of thick needles. The two substances were separated mechanically and recrystallized separately from alcohol. The compound which crystallized in rhombic tables melted at 105–6°.

Calc. for $C_{16}H_{13}O_3NBr_2$: C, 45.0; H, 3.0. Found: C, 45.3; H, 3.3.

The substance crystallizing in needles was obtained only in very small amounts. It was readily soluble in methyl and ethyl alcohols, moderately in ligroin, and melted at 91°.

Calc. for $C_{16}H_{13}O_3NBr_2$: C, 45.0; H, 3.0. Found. C, 45.8; H, 3.1.

The filtrates from the monobromo derivatives contained a small quantity of a dibromo compound which separated in crystalline form when they were allowed to evaporate very slowly in a cold place. By recrystallization from alcohol this was obtained in thin flakes melting 138–9°.

Calc. for $C_{16}H_{12}O_3NBr_3$: C, 38.0; H, 2.4. Found: C, 38.4; H, 2.6.

The two monobromo compounds melting at 115° and 106° must be stereoisomers because they give the same mono-iodo derivative when digested with potassium iodide. Neither of them undergoes further bromination even when heated with bromine in the sunlight. The third monobromo and the dibromo derivatives were obtained in quantities too small for further investigation.

γ-Nitro-γ-bromo - β - phenyl - propyl - (4 - bromophenyl)ketone, $CH_2(NO_2)BrCH(C_6H_5)CH_2COC_6H_4Br$.—Bromination in the position α to the nitro group was accomplished by means of the sodium derivative. This was made by adding the finely powdered nitro ketone to a concentrated solution of sodium methylate in methyl alcohol until some of it remained undissolved after vigorous shaking. The mixture was then filtered rapidly and the clear solution evaporated over sulfuric acid in a vacuum desiccator. It left a white solid which was powdered and extracted with dry ether to remove a small quantity of nitro ketone.

For the purpose of bromination, the dry powder was added very gradually to a well-cooled solution containing excess of bromine in dry carbon tetrachloride. The reaction was very vigorous but the yield of bromine compound was excellent. This was purified by allowing the solvent to evaporate spontaneously, washing the solid residue thoroughly with water, and recrystallizing from alcohol which contained a small quantity of benzene. The main product crystallized in needles and melted at 127°.

Calc. for $C_{16}H_{13}NO_3Br_2$: C, 45.2; H, 3.0. Found: C, 45.6; H, 3.2.

The filtrates deposited a small quantity of a second product which melted at 99–102°.

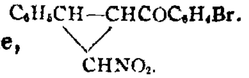
γ,γ-Dibromo-γ-nitro-β-phenyl-propyl-(4-bromophenyl) Ketone, $CBr_2NO_2CH(C_6H_5)CH_2COC_6H_4Br$.—The dibromo derivative was obtained without difficulty by alternately adding small quantities of sodium methylate and bromine to a cooled methyl alcoholic solution of the nitro compound, until both methylate and bromine were present in excess. The solid which separated was washed with water and cold alcohol, dried and recrystallized from a mixture of alcohol and benzene. It crystallized in thin plates or needles and melted, not sharply, at 144–6°.

Calc. for $C_{16}H_{12}O_3NBr_3$: C, 38; H, 2.4; Br, 47.4. Found: C, 38.8; H, 2.6; Br, 46.6.

Action of Potassium Iodide on the Bromo Derivatives.—It was shown in an earlier paper that it is possible to distinguish between bromine compounds in which bromine is a α to a nitro group and those in which it is α to a carbonyl by treatment with potassium iodide, the former undergoing reduction while the latter are transformed into the corresponding iodine derivatives. In order to determine whether this reaction is a general one, all the foregoing bromine compounds were boiled with potassium iodide in alcoholic solution. The γ-monobromo compound—which has bromine in the α-position to the nitro group, was quantitatively reduced to the nitro ketone. The γ,γ-dibromo compound was also reduced, giving first the monobromo compound melting at 127°, and finally the nitro ketone. The α-bromo compound gave the corresponding iodo compound in almost the calculated amount.

γ-Nitro-β-phenyl-α-iodo-propyl-(4-bromophenyl) Ketone, CH_2NO_2-$CH(C_6H_5)CHICOC_6H_4Br$.—Equal weights of the α-bromo compound and potassium iodide were dissolved in alcohol, and this solution boiled for 20 minutes. The mixture was then cooled and poured into a solution of sodium thiosulfate in order to remove a trace of iodine which had been liberated. The resulting flocculent precipitate was washed, dried and recrystallized from hot alcohol. It separated in pale yellow rhombic plates and melted at 110°. The same iodo compound was obtained by similar treatment of the lower melting α-bromo compound.

Calc. for $C_{16}H_{13}O_3NBrI$: C, 40.5; H, 2.7. Found. C, 40.6, H, 2.7.



$$\begin{array}{c}C_6H_5CH-CHCOC_6H_4Br.\\ \diagdown\ \diagup\\ CHNO_2.\end{array}$$

1-Nitro-2-phenyl-3(4-bromobenzoyl)cyclopropane, —For the purpose of eliminating hydrogen bromide from the α-bromo compound 12 g. of fused potassium acetate was added to a cooled suspension of 20 g. of the finely powdered bromo compound in 80 cc. of alcohol. The mixture was kept in ice water for 12 hours during which time most of the product separated as fine powder suspended in a brown liquid. The solid was filtered off, washed with alcohol and water until free from bromide, dried, and crystallized from alcohol containing a little benzene. One crystallization gave a pure product melting at 131°. Yield, 17 g., almost the calculated amount.

Calc. for $C_{16}H_{12}O_3NBr$· C, 55.5; H, 3.5; Br, 23.1. Found· C, 55.4; H, 3.7; Br, 22.9.

The cyclopropane derivative crystallizes in fine needles. It dissolves freely in acetone, carbon tetrachloride, benzene, and glacial acetic acid, sparingly in alcohol, and is almost insoluble in petroleum ether. Its solution in acetone does not reduce permanganate. It is more easily purified than the α-bromo compounds. For its preparation in quantity, therefore, it is advantageous to use in place of pure α-bromo compounds the crude mixture as it is obtained by brominating the nitro ketone in carbon tetrachloride and removing the solvent as completely as possible under diminished pressure.

An isomeric cyclopropane derivative was obtained by adding potassium acetate to an alcoholic solution of the γ-bromo bompound. The reaction takes place much more slowly than with the α-bromo compound, hence the mixture was allowed to remain at the ordinary temperature for 4 days. The precipitated solid was then washed and recrystallized from alcohol.

Calc. for $C_{16}H_{12}O_3NBr$· C, 55.5; H, 3.5. Found: C, 55.2; H, 3.6.

The substance crystallizes in fine needles and melts at 115°. It is probably formed as a result of the prolonged contact with potassium acetate because we found that the derivative melting at 130° is transformed into the lower melting isomer when its solution in alcohol is boiled for a short time with potassium acetate, or allowed to stand in contact with it for several days.

A third isomeric cyclopropane derivative is formed when an alcoholic suspension of either of the other two is treated with very dilute sodium methylate. Thus a solution of one g. of sodium in 10 cc. of methyl alcohol was added in small portions and with constant shaking to a suspenmethyl alcohol which was cooled in ice. The solid gradually dissolved and a new product began to separate from the pale yellow solution before all the alkali had been added. The cooling and shaking was continued until the whole volume of the alcohol was filled with solid. The solid was washed with cold alcohol until free from alkali, then recrystallized from boiling alcohol. The substance crystallized in needles and melted 162–3°. Its solution in acetone does not reduce permanganate. The same substance was obtained by treating the isomer melting at 115° in a similar manner.

Calc. for $C_{16}H_{12}O_3NBr$: C, 55.5, H, 3.4 Found. C, 55 3; H, 3.7.

Addition of Hydrogen.—The three isomeric cyclopropane derivatives readily combine with hydrogen when boiled with zinc dust and alcohol, and all three give the same product—the saturated open-chain nitro ketone. The following experiment illustrates the method used for adding hydrogen.

A suspension of 2 g. cyclopropane derivative and 5 g. of zinc dust in 80 cc. of 80% alcohol was boiled for a little more than an hour, then filtered while still hot to remove unchanged zinc and zinc oxide. The filtrate, on cooling, deposited colorless needles which melted at 101°. A mixture of the substance and the saturated nitro ketone melted at the same temperature.

Addition of hydrogen chloride.—The cyclopropane derivative melting at 130°, combined very readily with hydrochloric acid, and gave the calculated amount of addition product. An alcoholic suspension of the substance in a thick walled bottle was cooled in ice water and saturated with hydrogen chloride at 0°. The bottle was then securely stoppered and allowed to stand for 24 hours at the ordinary temperature. The crystalline suspension disappeared and the product separated as an oil which turned into a solid cake. This was crushed, washed until free from acid, and crystallized from alcohol and benzene.

Calc. for $C_{16}H_{13}O_3NClBr$: C, 50.2; H, 3.6. Found: C, 50.1; H, 3.4.

β-Nitro-γ,γ-phenyl-chloropropyl-(4-bromophenyl) Ketone, C_6H_5-$CHClCHNO_2CH_2COC_6H_4Br$.—The hydrochloric acid addition product crystallizes in long, slender needles which melt at 133°. It is readily soluble in chloroform, acetone, and benzene, sparingly in alcohol and ether, insoluble in ligroin. Alcoholic solutions gradually become strongly acid even at the ordinary temperature and at the boiling point of alcohol the addition product rapidly changes into other substances.

γ,γ-Phenyl-chloroallyl-(4-bromophenyl) Ketone, $C_6H_5CCl = CHCH_2$-COC_6H_4Br.—A suspension of 5 g. of the powdered chloro compound and 5 g. of potassium acetate in 25 cc. of alcohol was allowed to remain at the ordinary tmperature for 12 hours during which it changed to an aggre-

with cold alcohol and

water and dissolved in boiling alcohol. The solution yielded two substances in approximately equal amounts.

The first crop consisted mainly of a colorless substance which separated in downy needles and when pure melted at 179-80°. This substance contained no nitrogen, was sparingly soluble in alcohol but dissolved freely in chloroform, acetone and benzene.

Calc. for $C_{16}H_{12}OClBr$ C, 57.4; H, 3.6 Found: C, 58.2. H, 3.8.

Later crops consisted mainly of a yellow substance which was much more readily soluble in alcohol, separated in plates, and melted at 108-9°.

Calc. for $C_{16}H_{12}OClBr$ C, 57.4; H, 3.6. Found C 57.5, H, 3.9

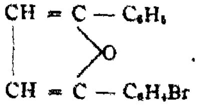
These substances are evidently geometrical isomers; they have the same composition, and reduce permanganate with equal ease—showing the presence of an ethylene linkage—and the chlorine is equally unreactive in both, indicating that in each it is connected with an unsaturated carbon atom. Definite proof of the structure of these substances was obtained by oxidation.

The substances rapidly reduced permanganate, but the only organic oxidation products that could be isolated were benzoic and *p*-bromobenzoic acids. It was necessary, therefore, to resort to ozone as oxidizing agent. Ozonized oxygen containing 3% ozone and a trace of moisture was slowly passed through a carbon tetrachloride solution of the yellow substance until ozone was present in excess. The solution gradually deposited a colorless solid, which melted at 244°. This was *p*-bromobenzoic acid—identified by melting a mixture of the substance with a sample on hand.

The filtrate from the bromobenzoic acid, when evaporated under diminished pressure, left a colorless oil which attacked the eyes and had the odor of benzoyl chloride. The liquid was dissolved in dry ether and treated with excess of aniline. This gave a solid which after recrystallization from boiling alcohol melted at 160° and was identified as benzanilide. The principal oxidation products of the yellow compound are, therefore, benzoyl chloride and *p*-bromobenzoic acid. The white isomer, treated in the same way, gave the same products.

These results establish the structure of the hydrochloric acid addition product as well as that of the unsaturated chloro ketones obtained from it. The structure of the latter was determined with great care because this mode of loss of nitrous acid, in which the hydrogen comes from the γ- instead of the α-position was unexpected.

$$C_6H_5CHClCHNO_2CH_2COC_6H_4Br \longrightarrow C_6H_5CCl = CH - CH_2COC_6H_4Br.$$



1-Phenyl-5-(4-bromophenyl) Furane, . — The hythe bromine free analog rapidly lost both hydrochloric and nitrous acids when boiled in alcoholic solution. The product separated in almost the calculated quantity when the solution was allowed to cool.

Calc for $C_{16}H_{11}OBr$. C, 64.2; H, 3.7 Found: C, 64.1; H, 4.0.

The furane derivative crystallizes in colorless or very pale yellow flakes, and melts at 127°. It is very sparingly soluble in alcohol and ether, more readily in acetone and benzene. Its solution in acetone does not reduce permanganate.

Addition of Hydrogen Bromide.—The cyclopropane derivatives gave two isomeric addition products depending upon the manner in which the addition was brought about. When either the substance melting at 130°, or its isomer melting at 162°, is added to glacial acetic acid which has been previously saturated with hydrogen bromide, it dissolves rapidly, the product begins to separate almost immediately and the reaction is complete in a few minutes. The substance obtained in this way was purified by recrystallization from benzene-ligroin and was thus obtained in colorless needles which melted with decomposition at 144°.

Calc. for $C_{16}H_{13}O_3NBr_2$· C, 45 0; H, 3 0 Found C, 44 8; H, 3 3

Each of the two cyclopropane derivatives gave an isomeric substance when solutions in glacial acetic acid were gradually saturated with hydrogen bromide at 0° and then allowed to stand for 12 hours. The product in this case separated in long needles which after crystallization from benzene-ligroin melted at 133°.

Calc. for $C_{16}H_{13}O_3NBr_2$ C, 45 0, H, 3 0. Found. C, 44 9; H, 3 0

Both of these addition products when boiled with alcohol give the same 1-phenyl-5-(4-bromophenyl) furane; they are, therefore, constituted like the corresponding hydrogen chloride addition product.

γ-Phenyl-β-nitro-alkyl-(4-bromophenyl) Ketone, $C_6H_5CH = CNO_2$-$CH_2COC_6H_4Br$.—Unlike the hydrogen chloride addition product, the bromine compound loses halogen acid more easily than nitrous acid. Thus when 10 g. of the substance and 5 g. of potassium acetate were suspended in 30 cc. of alcohol, the substance dissolved rapidly, the solution turned light brown in color and a colorless product separated in a short time. This was washed, dried and recrystallized from a mixture of carbon tetrachloride and ligroin from which it separated in colorless needles, melting, with decomposition, at 162–3°.

Calc. for $C_{16}H_{12}O_3NBr$: C, 55.5; H, 3 5. Found: C, 56.5; H, 3.6.

The substance is extremely unstable, and the high values are doubtless due to loss of nitrous acid during purification.

Addition of Bromine.—The cyclopropane derivatives are not at- [illegible] temperature even when exposed to direct sunlight. A slow but complete reaction can be obtained, however, under the combined effect of heat and direct sunlight, provided both the reagents and the solvent are perfectly dry.

α,γ-Dibromo-β-phenyl-propyl-(4-bromophenyl) Ketone, $C_6H_5CHBrCHNO_2CHBrCOC_6H_4Br$.—A saturated carbon tetrachloride solution containing 33 g. of the cyclopropane derivative melting at 130° and 17 g. of bromine were boiled in the sunlight for several days. The only evidence of reaction was a slow deposition of solid from the hot solution, and the boiling was continued as long as this appeared to increase in quantity. The solid was recrystallized from carbon tetrachloride. This gave 33 g. of a colorless product which melted at 162–3°.

Calc for $C_{16}H_{12}O_3NBr_3$: C, 37.9; H, 2.4 Found: C, 37.6; H, 2.6

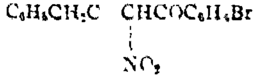
The filtrate from this substance on slow evaporation deposited two more solid products. These were separated by recrystallization from benzene. The more soluble of the two crystallized in rhombic plates which melted at 137°. The analyses show that this is an isomeric bromine addition product.

Calc. for $C_{16}H_{12}O_3NBr_3$. C, 37.9; H, 2 4 Found C, 38.2; H, 2.5.

These two bromine addition products were obtained by another reaction that leaves no doubt as to their structure. The γ-bromo compound obtained by adding hydrogen bromide to the cyclopropane derivative readily reacts with bromine, as would be expected, and the two products of the reaction are identical with those obtained by addition of bromine to the cyclopropane derivative:

$$C_6H_5CHBrCHNO_2CH_2COC_6H_4Br + Br_2 = C_6H_5CHBrCHNO_2CHBr\ COC_6H_4Br.$$

γ-Phenyl-β-nitro-propenyl-(4-bromophenyl) Ketone,



$C_6H_5CH{:}C\ \underset{NO_2}{C}HCOC_6H_4Br$

.—The bromine addition products are reactive substances but they gave unmanageable mixtures with nearly all reagents capable of replacing bromine or of eliminating hydrogen bromide. Potassium iodide was an exception, as it gave a crystalline product in good yields. Four g. of potassium iodide was added to a solution of 2 g. of the bromine compound (162°) which had been cooled to 0°. Iodine began to separate at once. The solution was allowed to remain in an ice chest for 2 days, then evaporated in a current of air. The residue was washed with thiosulfate solution, dried, and recrystallized from alcohol and benzene. It crystallized in yellow plates and melted at 115°.

Calc. for $C_{16}H_{12}O_3NBr$: C, 55 4; H, 3.4. Found: C, 55.4; H, 3.9.

The substance is moderately soluble in alcohol, readily in benzene, acetone, and chloroform ganate. The oxidation products, phenylacetic acid melting at 76° and *p*-bromo-benzoic acid, were identified by comparison with specimens on hand. The third product of the reaction between bromine and the cyclopropane derivative was obtained as a very fine crystalline powder which is sparingly soluble in benzene and alcohol and which melts at 190-3°.

Calc. for $C_{16}H_{12}Br_4O$. C, 35.6; H, 2.2. Found: C, 35.8; H, 2.2.

The substance contains no nitrogen. It is very unreactive, undergoing no change when boiled with alcoholic potassium acetate or sodium alcoholate. It is, therefore, probably a furane derivative formed by loss of nitrous acid during the protracted boiling and addition of bromine to the product[1] but the facts at hand do not warrant a definite conclusion.

Action of Sodium Methylate.—As was stated earlier in the paper, dilute sodium methylate turns the lower melting cyclopropane derivatives into the highest melting isomer and the concentrated methylate as well as sodium hydroxide gives a β-diketone. A possible intermediate product in this reaction was obtained as follows: A solution of 5 g. of sodium in the minimum quantity of dry methyl alcohol was added to 60 g. of the finely powdered cyclopropane derivative (130°) previously moistened with a little dry methyl alcohol. The temperature of the mixture was kept at 0° throughout the addition. The cyclopropane derivative slowly dissolved, sodium nitrite deposited on the walls of the vessel while another white solid crystallized from the red solution. The mixture was kept at 0° for several hours, then cooled in a freezing mixture and acidified with a solution of the calculated amount of glacial acetic acid in 300 cc. of ether.

The resulting paste which changed from red to yellow during acidification, was poured into cracked ice contained in a separatory funnel, the ethereal layer washed with water, dried, and allowed to evaporate. The residue contained 8 g. of a colorless solid contaminated with a small quantity of yellow oil. The solid was purified by recrystallization from methyl alcohol.

Calc. for $C_{17}H_{15}O_2Br$: C, 61.6; H, 4.6. Found: C, 61.3; H, 4.6.

The substance is readily soluble in alcohol and ether. It crystallizes in thin needles and melts at 102-3°. Its structure was established by oxidation with permanganate which was carried out as follows: 2.5 g. of finely powdered potassium permanganate was added in very small portions to a solution of 3.2 g. of the substance in pure acetone, which was kept at 0° until the reduction of the permanganate was complete. The salts and oxides of manganese were filtered off and the filtrate evaporated under diminished pressure. It left a small quantity of solid imbedded in an oil that had the odor of methyl phenylacetate.

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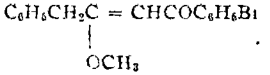
[1] Perkins, *J. Chem. Soc.*, 57, 954 (1890).

The oil was distilled with steam and hydrolyzed with potassium hydroxide. It gave a solid acid which melted at 76°. A mixture of the substance and phenyl acetic acid likewise melted at this temperature. The oily oxidation product was, therefore, methyl phenylacetate.

The solid left behind after removing the ester by steam distillation proved to be unchanged substance, and the acid obtained by treating the salts and oxides of manganese with sodium hydrogen sulfite and dilute acid was identified as bromo-benzoic acid. These oxidation products —methyl phenylacetate and *p*-bromo-benzoic acid—show that the formula of the methoxy compound must be



$$\underset{\displaystyle OCH_3}{C_6H_5CH_2\overset{}{C}} = CHCOC_6H_6Br \quad .$$

Phenacetyl-(4-bromobenzyl) Methane, $C_6H_5CH_2COCH_2COC_6H_4Br$.—The methoxyl compound is easily hydrolyzed when boiled with a few drops of hydrochloric acid in aqueous alcohol. The product separated, on cooling, in rhombic plates melting at 80-1°.

Calc for $C_{17}H_{15}O_2Br$ C, 60 5, H, 4.1. Found C, 60 4; H, 4.3.

The diketone is readily soluble in all common organic solvents except ligroin When its ethereal solution is shaken with an aqueous solution of copper acetate it forms a pale green copper derivative which is sparingly soluble in ether but dissolves fairly readily in benzene. The diketone can be obtained directly from any of the cyclopropane derivatives by dissolving it with alcoholic sodium hydroxide, acidifying, extracting with ether, and precipitating the diketone as copper derivative.

CAMBRIDGE MASS

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF MICHIGAN.]

TRIPHENYLMETHYL. XXIX. A STUDY OF THE PROPERTIES OF DIPHENYL-α-NAPHTHYLMETHYL.

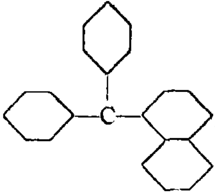
BY M GOMBERG AND C. S. SCHOEPFLE [1]

Received July 22, 1919.

1. Introduction.

Although the existence of a large number of triarylmethyls has been established, the various investigators in this field have been content to prepare the free radicals in solution only and to show that such solutions on exposure to air give rise to the corresponding peroxides. In a limited number of cases the triarylmethyls were actually isolated and the molecular weight of the free radical determined, and in a few instances absorption spectra have been taken. But in no case except that of triphenylmethyl have the chemical and physical properties of the free

[1] The work described in this article and in the article published in THIS JOURNAL, 39, 1652 (1917), forms part of a thesis presented

radical been thoroughly investigated. The question arises: Are all the peculiar physical and chemical properties of triphenylmethyl characteristic of the triarylmethyls as a class, or do some of them apply only to certain individuals in this class? It therefore seemed desirable to study carefully and fully other members of the triarylmethyls, and thus compare their properties and reactions with those of triphenylmethyl. For this purpose the radical diphenyl-α-naphthylmethyl, , was chosen as it is readily prepared and can be obtained in very pure state. Moreover, it gave promise of most interesting results for it was known, according to preliminary experiments,[1] to exist in solution largely in the mono-molecular phase. Being thus much more highly dissociated, diphenyl-α-naphthylmethyl presumably should show a correspondingly greater degree of unsaturation than triphenylmethyl, and should exhibit a greater reactivity than the latter. In what way would this affect the peroxide factor, and the equilibrium with iodine? And would this free radical give additive compounds more stable than those given by triphenylmethyl? Would it isomerize under the influence of hydrochloric acid similarly to triphenylmethyl?

The exact knowledge of the molecular state of diphenyl-α-naphthylmethyl was considered of utmost importance, since it is the tendency towards dissociation into half-molecules that imparts to the hexa-arylethanes their distinctive reactivity. A comparison of the molecular state of aggregation of diphenyl-α-naphthylmethyl with that of triphenylmethyl should permit one to judge whether the extent of actual dissociation, *i. e.*, the relative amount of free radical actually present, is really the cause for the difference in chemical reactivities of the triarylmethyls among themselves.

The molecular state of these compounds has received more attention than any other single attribute, for the reason that this was supposed to furnish the conclusive answer to the query—can carbon function in the trivalent state? But the number of free radicals, the molecular state of which has been determined with exactness, is after all limited. None the less, it may be considered at the present time as fairly well established that the molecular state of triarylmethyls is best represented by the general expression which covers both the tautomerization phenomenon and the dissociation phenomenon:[2]

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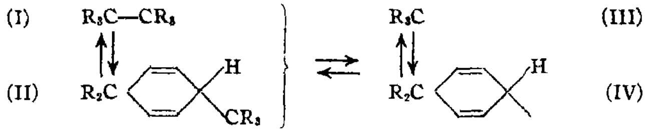
[1] This Journal, 39, 1668 (1917).

[2] *Ber.*, 46, 228 (1913).



In other words, there is a tautomeric equilibrium between two dimolecular modifications, the benzenoid hexa-aryl ethane (I) and its quinonoid modification (II); also between two monomolecular modifications, the benzenoid triarylmethyl (III), wherein the central carbon atom is trivalent, and the quinonoid modification (IV), in which the *para*-carbon atom assumes the trivalent state. The experimental evidence upon which is based the assumption of the existence of a tautomeric pair in the dimolecular and in the monomolecular phases of the triarylmethyls has been dealt with in previous papers. The validity of that evidence has not been impaired, in our opinion, by any subsequent results. The new experimental evidence contributed in this paper deals with the dissociation phenomenon only and has no direct bearing on the tautomerism phenomenon. For this reason, the tautomerism question will be left out of consideration for the sake of simplicity in the following discussion; the dissociation phenomenon alone will be considered, and as if occurring only in the following sense:

$$R_3C - CR_3 \rightleftarrows 2R_3C.$$

Factors Influencing Degree of Dissociation.—It is evident that the extent of the dissociation must differ, primarily, with the nature of the free radical. Triphenylmethyl exists largely in the dimolecular state, but triarylmethyls containing biphenyl groups are monomolecular to the extent of 15%, 80%, and 100%, respectively, according to the number of biphenyl groups in the molecule.[1] The hypothesis, however, that the dissociation of the hexa-aryl ethanes is proportional to the complexity of the aryl groups has been shown to be untenable. From the study of the molecular weights of a selected group of triarylmethyls it was found impossible to formulate the relation between the complexity of the aryl groups on the one hand and the tendency of these ethanes towards dissociation into free radicals on the other.[2]

Other factors which may influence the equilibrium between the monomolecular and the dimolecular modifications in solution, are the nature of the solvent, the concentration of the solute, and the temperature of the solution. The question as to whether the nature of the solvent exerts an influence on the extent of dissociation could only be finally settled by a set of molecular weight determinations on a given triarylmethyl in various solvents which freeze approximately at the same temperature. But it is doubtful whether this factor is of appreciable influence, barring of course such instances where chemical combination between solute and solvent occur. We have assumed that this influence is practically negligible, and the results herein described support this assumption.

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[1] Schlenk, Weickel and Herzenstein, *Ann.*, **394**, 186 (1912); *Ber.*, **43**, 1756 (1910); *Ann.*, **372**, 4 (1909); Schmidlin and Garcia-Banus, *Ber.*, **45**, 3176 (1912).

[2] This Journal, **39**, 1672 (1917).

Piccard,[1] Schmidlin,[2] and others have studied by different methods the effect of the concentration upon the degree of dissociation of the hexa-arylethane in solution. The writers[3] have determined with painstaking accuracy the molecular weight of 7 different triarylmethyls in naphthalene as a solvent, with concentrations ranging from 1 to 6%. The results obtained show unmistakably that, in every case, the dissociation of the hexa-aryl ethanes into free radicals increases with dilution of the solute, and in some cases reaches 100%. It remained to study the third factor which must influence the equilibrium between the monomolecular and the dimolecular phase of the free radical, namely the effect of temperature. Some work in this respect has been done in the past, but mostly of qualitative nature.[4] We have now, with this end in view, determined very carefully the molecular weight of diphenyl-α-naphthyl methyl in a number of different solvents whose freezing points cover a wide range of temperature, 5° to 80°. The results, it is believed, settle the mooted question as regards the decided increase of dissociation with increase of temperature, at least in the instance of this particular free radical.

The object, then, of this investigation has been: (1) having selected a compound possessing a considerably greater degree of dissociation than triphenylmethyl, to determine whether this attribute would be accompanied by an enhancement of the various chemical characteristics typical to triphenylmethyl; (2) to determine with a high degree of accuracy the molecular weight of this free radical in various solvents covering a wide range of temperature, in order to ascertain the influence of temperature on the molecular state of the free radical.

2. Chemical Reactions of Diphenyl-α-naphthylmethyl.

Preparation of Diphenyl-α-naphthylmethyl Chloride.—Attempts were made to prepare the required diphenylnaphthylmethyl chloride by the Friedel and Crafts' reaction, condensing benzophenone chloride with naphthalene. The diphenylnaphthylmethyl chloride thus obtained is almost colorless, and upon one recrystallization melts sharply at 169°. The yield, however, is never more than 20%. The use of ferric chloride in place of aluminium chloride gave no better results.

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[1] *Ann.*, 381, 347 (1911).

[2] "Das Triphenylmethyl," Ferdinand Enke, 1914, p. 67.

[3] THIS JOURNAL, 39, 1664 (1917).

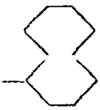
[4] Schlenk and Mair, *Ann.*, 394, 179 (1912); Schmidlin, *Ber.*, 45, 3180 (1912).

An attempt was next made to apply a modified Grignard reaction, namely to combine benzophenone chloride with α-naphthyl magnesium bromide. But this gave an impure product which could not be crystallized either as the carbinol or the chloride even after purification by boiling with charcoal. Consequently it was decided to revert to the regular Grignard reaction, employing benzophenone and α-naphthyl magnesium bromide. This gives about an 80% yield of diphenylnaphthyl carbinol. To obtain the corresponding chloride, the carbinol is dissolved in benzene and the amount of acetyl chloride required to replace the hydroxy group by chlorine is added. Upon concentrating the solution, the diphenylnaphthylmethyl chloride is obtained in large, colorless crystals which melt at 170–171°. The product was always recrystallized from benzene to remove any traces of acid.

If the solution of diphenyl-α-naphthyl carbinol is treated with acetyl bromide in place of acetyl chloride, the corresponding bromide is formed. The crystals are colorless and melt at 165–166°, with slight decomposition. The bromide is quite stable and agrees with the chloride in all its properties

Calc for $C_{23}H_{17}Br$ Br, 21.4. Found: 21.6

By treating a solution of diphenyl-α-naphthylmethyl chloride in absolute alcohol with sodium ethoxide, or by passing hydrogen chloride into an alcoholic solution of either the carbinol or the chloride, diphenylnaphthyl ethyl ether is obtained in well-defined, colorless crystals which melt at 132°.

The Free Radical, $(C_6H_5)_2C$—.—To prepare the free radical, 4 g. of diphenyl-α-naphthylmethyl chloride and 4 g. of molecular silver are placed in a 100 cc. bottle, and enough dry benzene added to almost fill the bottle which is then tightly corked. After several hours' shaking, the reaction is complete. The cork is now removed, and there is quickly inserted the glass connection which permits the siphoning off of the clear liquid into the standard apparatus which has been fully described in previous papers.[1] The benzene is distilled off under reduced pressure and the product recrystallized from hot acetone, air of course being excluded. The solvent is drawn off and the crystalline diphenylnaphthylmethyl is washed several times with acetone, and then dried under reduced pressure in a slow stream of carbon dioxide, the crystals remaining all the while in the same apparatus. As a rule, from 1.5 to 2 g. of the free radical was obtained, the yield being sacrificed to favor a purer product.

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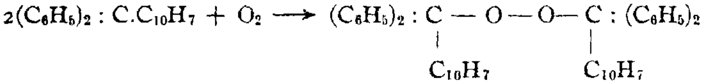
[1] Gomberg and Cone, *Ber*, 37, 2033 (1904), Gomberg and Schoepfle, THIS JOURNAL, 39, 1659 (1917).

The solution of diphenylnaphthylmethyl has a deep reddish brown color, but the crystals obtained are practically colorless, becoming light yellow upon standing. When heated in an atmosphere of carbon dioxide, they turn brown at about 130° and melt at 135–137°, although the melting point is not sharp.

Action of Oxygen.—When the deeply colored solution of diphenylnaphthylmethyl is exposed to oxygen or air it is rapidly decolorized and a crystalline peroxide is formed. Diphenylnaphthylmethyl peroxide is practically insoluble in ether, petroleum ether or benzene, but is slightly soluble in hot carbon disulfide from which it crystallizes in very fine, colorless crystals, melting at 172–173° with decomposition.

In the formation of the peroxide, the theoretical amount of oxygen is absorbed in accordance with the equation:



$$2(C_6H_5)_2:C.C_{10}H_7 + O_2 \longrightarrow (C_6H_5)_2:\underset{C_{10}H_7}{\underset{|}{C}}-O-O-\underset{C_{10}H_7}{\underset{|}{C}}:(C_6H_5)_2$$

The apparatus used in measuring the absorption of oxygen by triarylmethyls has been described in detail in a previous paper.[1] It consists of a 175 cc. absorption bottle which is connected with a water-jacketed gas buret provided with a leveling tube containing bromobenzene. A weighed sample of diphenylnaphthylmethyl chloride and an equal amount of molecular silver are put in a small test tube which is then filled with bromobenzene and quickly sealed. After several hours' shaking, the tube is placed in the absorption bottle, covered with about 25 cc. of bromobenzene, and the bottle sealed with paraffin and submerged in a large pail of water which is kept at the desired temperature. The apparatus is now filled with dry oxygen, and after the temperature has become constant, the bottle is shaken to break the tube. The absorption is measured by means of the buret, and calculated on the basis that the diphenylnaphthylmethyl chloride taken had given the theoretical amount of free radical. During the course of the experiment, the temperature of the bottle and the buret was kept constant while corrections were applied to allow for changes in barometric pressure.

As in the case of triphenylmethyl, the absorption proceeds at a very rapid rate, being complete within a few minutes if sufficient bromobenzene is used to keep all of the free radical in solution (Expts. 1–3).

We have also determined the amount of oxygen absorbed when the crystalline free radical is similarly treated. The sample in the form of pellets was put in a small test tube which was then filled with bromobenzene and quickly sealed. The amount of absorption was somewhat smaller in this case than in the preceding experiments, doubtless due to a slight oxidation which took place during the time required for sealing the tube (Expts. 4 and 5).

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[1] THIS JOURNAL, 39, 1661 (1917).

		Wt of sample		Oxygen absorbed.[1]	
		Diphenyl napthylmethyl chloride G	Diphenyl naphthylmethyl G	Cc	% of calculated.
1	With oxygen	1 000		33 0	97
2	With oxygen	1 013		34 2	99
3	With air	1 011		32 7	95
4	With oxygen		1 029	36 2	92
5	With oxygen		1 142	40 7	93

In spite of the fact that the theoretical amount of oxygen is absorbed, diphenylnaphthylmethyl, like triphenylmethyl, does not give the theoretical amount of peroxide. To determine the amount of peroxide formed, the sample of the free radical was dissolved in ether and oxidized by passing air through the solution. The precipitated peroxide was transferred to a modified Gooch crucible, washed with ether, then dried and weighed.

	Wt of diphenylnaphthylmethyl G	Wt of peroxide G	% of theoretical amount.
1	1 280	1 160	86
2	1 251	1 133	86
3	1 595	1 446	86

Therefore, for diphenylnaphthylmethyl we have a remarkably constant peroxide factor of 86%. If benzene is used as the solvent in place of ether, the factor is somewhat lower varying from 80% to 82%.

Absorption of Iodine.—If a solution of iodine in benzene or carbon disulfide is added to a solution of diphenylnaphthylmethyl, the dark color of iodine instantly disappears, and the absorption of iodine continues until approximately 60% of the free radical has been titrated. A weighed sample of diphenylnaphthylmethyl is placed in a bottle from which the air is completely removed by successively exhausting and filling with carbon dioxide. Enough bromobenzene is added to dissolve the free radical (the free radical is more soluble in bromobenzene than in benzene) and then a standard solution of iodine in benzene is slowly added. The deep reddish brown color of the solution gradually becomes lighter and at the equilibrium point, which is fairly distinct, the color changes from the light brown of the free radical to a deep green, the latter color resulting doubtless from the presence of both iodine and the free radical in the solution.

	Wt of diphenylnaphthylmethyl. G	Cc of 0 1 *N* iodine solution absorbed	% of calculated absorption.
1	2 406	50 5	61.5
2	2 565	49 0	56 0
3	2 147	46 0	63 0

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[1] Corrected to standard conditions of temperature and pressure.

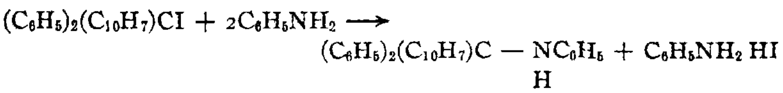
Therefore, an equilibrium is established when approximately 60% of the diphenylnaphthylmethyl has been changed to diphenylnaphthylmethyl iodide.

$$(C_6H_5)_2C\cdot C_{10}H_7 + I \rightleftarrows (C_6H_5)_2(C_{10}H_7)CI$$

Attempts to Isolate the Iodide.—Attempts were made to isolate the diphenylnaphthylmethyl iodide from the solution obtained by titrating the free radical with a limited amount of iodine as described above, but in no case would the iodide crystallize. Efforts to prepare the iodide by a somewhat different method[1] also proved unsuccessful. 5 g. of diphenylnaphthylmethyl chloride and 2.5 g. of sodium iodide were dissolved separately in acetone, and mixed in an apparatus free from air. The sodium chloride which immediately precipitated out was filtered off and the solution concentrated but the iodide could not be isolated. A considerable amount of diphenylnaphthyl methane was found to be present in the solution, indicating that the free radical and perhaps the iodide as well, have suffered a change of some sort. The iodide under *consideration is therefore even more unstable than triphenylmethyl* iodide.

If excess of iodine is added to the solution of the free radical, a dark oil separates out which is undoubtedly a periodide. This periodide could not be crystallized and is apparently unstable, as it is changed into soluble products upon standing for several hours. The resulting solution, as in the above experiments, contains a considerable amount of diphenylnaphthyl methane, and no longer precipitates a peroxide on exposure to air.

That diphenylnaphthylmethyl iodide is actually formed by the action of iodine upon a solution of the free radical, was shown by the preparation of the corresponding anilide. To a solution of 4 g. of diphenylnaphthyl methyl in benzene was added 65 cc. of a 0.1 *N* solution of iodine in benzene, which corresponds to about 50% of the theoretical amount of iodine required to change the free radical into the iodide. 2 g. of aniline was then added, producing an immediate precipitation of aniline hydriodide.



$$(C_6H_5)_2(C_{10}H_7)CI + 2C_6H_5NH_2 \longrightarrow (C_6H_5)_2(C_{10}H_7)C - \underset{H}{N}C_6H_5 + C_6H_5NH_2.HI$$

After standing for a short time, air was passed through the solution to oxidize the unchanged free radical to the peroxide. The aniline salt and the peroxide were filtered off, the benzene removed under reduced pressure, and the residue taken up in petroleum ether. 2.3 g. of diphenylnaphthylmethyl anilide crystallized, the theoretical yield being 2.5 g. The anilide is obtained in clusters of small, colorless crystals which after several recrystallizations melt at 151°. The compound was found to be identical with the anilide prepared similarly from diphenylnaphthylmethyl chloride. The anilide is readily decomposed into aniline and diphenylnaphthylmethyl chloride when a benzene solution of it is treated with hydrogen chloride.

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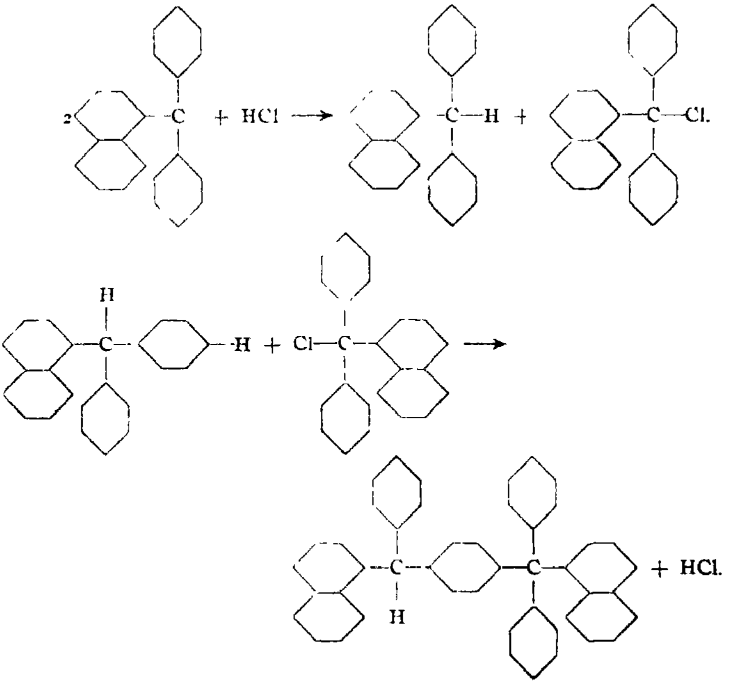
[1] Albrecht, "Das Triphenylmethyl," Schmidlin, Ferdinand Enke, 1914, p. 87.

Action of Hydrochloric Acid.—When a solution of diphenylnaphthylmethyl is treated in the cold with hydrochloric acid, it is decolorized, becoming absolutely colorless in the course of several hours. The resulting solution contains diphenylnaphthyl methane and diphenylnaphthylmethyl chloride, along with a smaller amount of the "polymer" of the free radical, indicating that the following two reactions have occurred:



(1)

(2)

The extent tó which each reaction takes place was determined by estimating the amount of diphenylnaphthylmethyl chloride which could be obtained from a definite amount of the free radical. The sample of diphenylnaphthylmethyl, 2.4625 g., prepared as usual, was treated in the absence of air with about 150 cc. of benzene saturated with hydrochloric acid. After the free radical was dissolved and the solution had become colorless, the benzene was removed under reduced pressure; the sample was then redissolved in benzene and again concentrated as far as possible, thus insuring the removal of the excess hydrochloric acid. The chlorine in the residue was estimated in the usual manner. The amount found corresponded to 83% of the amount of diphenylnaphthylmethyl chloride which would have been formed had all the free radical reacted according to Equation 1. Therefore, it may be safely inferred, over 80% of the diphenylnaphthylmethyl reacts to give diphenylnaphthyl methane and diphenylnaphthylmethyl chloride, and the remainder probably reacts according to Equation 2 to form the polymer of diphenylnaphthylmethyl.

To obtain the polymer, 10 g. of diphenylnaphthylmethyl chloride is dissolved in 150 cc. of benzene saturated with hydrochloric acid, and shaken with excess of molecular silver, about 20 g. The solution immediately becomes deeply colored due to the formation of the free radical, and this subsequently reacts with the hydrochloric acid. The diphenylnaphthylmethyl chloride which is formed as one of the products of the action of the hydrochloric acid upon the free radical, is in turn acted upon by the molecular silver, and so on to completion. The solution becomes colorless after several hours' shaking, and contains then only diphenylnaphthyl methane and the polymer, of which the former is present in much the larger amount. The polymer can be readily separated from the diphenylnaphthyl methane by treating the mixture with boiling alcohol, in which the methane compound is fairly soluble and the polymer practically insoluble. The yield is about 3 g.

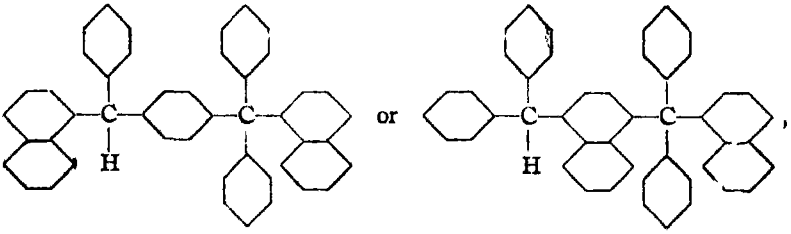
In solubility the polymer is very similar to *p*-benzohydryltetraphenyl methane, which is the principal product when triphenylmethyl is treated with hydrochloric acid.[1] It is readily soluble in hot benzene, slightly soluble in hot acetic acid, and practically insoluble in alcohol, ether, and petroleum ether. It crystallizes from benzene upon the addition of petroleum ether in very fine, colorless crystals which melt at 234–235°.

Calc. for $C_{46}H_{34}$: C, 94.15; H, 5.85. Found: C, 93.81; H, 5.92.

The molecular weight, determined by the cryoscopic method with naphthalene as the solvent, was found to be abnormal. 0.3615 g. of the polymer in 16.86 g. of naphthalene (K = 70.8), gave a depression of 0.354°.

Calc. for $C_{46}H_{34}$: M, 586. Found: M, 429.

No attempt was made to determine which of the two possible structures



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[1] Gomberg, *Ber.*, **35**, 3914 (1902); **36**, 376 (1903).

should be assigned to this compound, assuming that the polymerization in this case is identical in character with that of triphenylmethyl under similar circumstances.[1]

Reduction of the Free Radical.—Although hydrogen itself has no action upon a solution of diphenylnaphthylmethyl, in the presence of a catalyst, such as platinum black, reduction to diphenylnaphthyl methane takes place quite readily. The platinum black for this purpose was prepared by reducing platinum tetrachloride with formaldehyde in an alkaline solution.

A solution of 5 g. of the free radical in benzene was siphoned into a flask filled with hydrogen and containing 0.5 g. of platinum black. The solution, diluted with ether, was stirred vigorously. It absorbed hydrogen readily, becoming completely decolorized in the course of two hours. The platinum was filtered off, the solution concentrated, and the residue taken up in ether from which practically the theoretical amount of diphenylnaphthyl methane crystallized.

Attempts to Prepare Additive Compounds of the Free Radical.—In the experiments to form additive compounds of diphenylnaphthylmethyl the procedure followed was similar to that adopted in the preparation of the additive compounds of triphenylmethyl. After the benzene solution of the free radical had been concentrated as far as possible in the apparatus previously described, about 50 cc. was added of the compound, the additive tendency of which was to be investigated, and the clear solution was allowed to crystallize overnight. The mother liquid was drawn off, and the crystals washed and then dried under reduced pressure in a slow stream of carbon dioxide. A sample of the compound, usually from 1.5–2 g., was weighed out in a porcelain boat, placed into a glass tube about 40 cm. long and heated under reduced pressure in an air bath at 80–100° for one to two hours, a slow stream of carbon dioxide being passed at the same time through the tube. The loss in weight of the sample in the boat should represent in each case the amount of the solvent in combination with the free radical, provided combination between the free radical and the solvent had occurred. That the material suffered no appreciable decomposition as the result of the heating, was shown by the fact that at the end of the experiment it still absorbed 80–85% of the theoretical amount of oxygen.

The action of the following solvents was investigated, at least two experiments, and more often three, being carried out with each solvent.

Ethers	Ethyl ether
	Amyl-ethyl ether
Esters	Amyl formate.
	Ethyl acetate
	Amyl acetate

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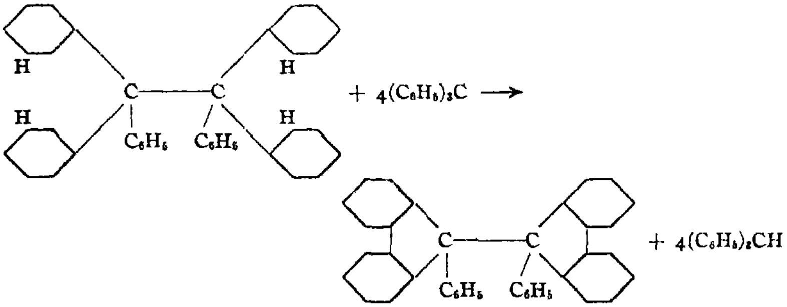
[1] Chichibabin, *Ber.*, 37, 4709 (1904); 41, 2421 (1908).

	Ethyl chloroacetate.
	Ethyl valerianate.
Ketones..	Acetone.
	Dipropyl ketone.
	Methyl-butyl ketone.
Nitriles	Acetonitrile
	Propionitrile.
Hydrocarbons	Benzene.
	Toluene.
	Xylene.
	Caprylene.

No addition of diphenylnaphthylmethyl with any solvent took place. This is in marked contrast to the action of triphenylmethyl.

Action of Light.—A solution of diphenylnaphthylmethyl when exposed to sunlight gradually loses color, the autoöxidation being exceedingly slow. Solutions of the free radical in benzene and bromobenzene which have been exposed to light for 15 months still retain to a slight extent the color of the free radical. This is in contrast to solutions of triphenylmethyl which are quite susceptible to light and become colorless after a few hours' exposure, due to the formation of triphenyl methane and dibiphenylene-diphenyl ethane.[1]



A solution of diphenylnaphthylmethyl which had been exposed to light was found to contain a considerable amount of diphenylnaphthyl methane, it seems probable therefore that the reaction proceeds in a manner similar to that in the case of triphenylmethyl

3. Molecular-Weight Determinations of the Free Radical.

Apparatus and Manipulation.—The molecular weight of diphenylnaphthylmethyl was determined by the cryoscopic method using 5 different solvents. The apparatus was of the type devised by Beckmann in which a 2-ring stirrer is used, the upper ring being of wrought iron covered with platinum. This is attracted by an electromagnet attached on the outside of the freezing vessel, and rises and falls due to the alternate making and breaking of the current, effected by a metronome. The apparatus, as adapted by us for the purpose of the molecular-weight determination of triarylmethyls, has been described in detail in a previous paper.[1] The manipulation for the handling and introducing of the free radicals as there described has also been followed in the present case, with hydrogen as the inert gas to guard against oxidation.

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[1] Gomberg and Cone, *Ber*, 37, 3546 (1904); Schmidlin and Garçia-Banus, *Ibid.*, 45, 1345 (1912).

Selection of Solvents.—Since the primary object of these experiments was to obtain the molecular weight of diphenylnaphthylmethyl at different temperatures, it was attempted to select a series of solvents whose freezing points varied uniformly from 0° to about 90°. The selection of such a series proved extremely difficult, since, in the first place, the free radical is but slightly soluble in many of the solvents ordinarily suitable for cryoscopic determinations, especially those freezing at fairly low temperatures, and secondly, many of the more common solvents do not lend themselves sufficiently to the degree of accuracy required. For example, ethylene dibromide, dimethyl aniline, dimethyl oxalate and benzene can not be used because of the slight solubility of the free radical in these solvents.[2] α-Bromonaphthalene, benzophenone, *m*-bromonitrobenzene, and azobenzene were found to be unsuited for accurate determinations, due partly to the readiness with which they supercool, and partly to the fact that from 5 to 8 minutes are required after the solution has started to freeze for the temperature to reach the highest point. Still another difficulty was encountered in the case of *p*-dibromobenzene. Although this proved to be an excellent solvent and in general well suited for accurate determinations, it was found that the freezing point of the solution of the free radical did not remain constant but rose steadily with successive determinations showing that some manner of decomposition was taking place, due probably to the relatively high temperature of its freezing point, 87°. Therefore, experiments with this solvent were necessarily abandoned.

After considerable preliminary investigation, the following series of solvents were selected:

	F. P.
Nitrobenzene	6°
p-Bromotoluene	27°
p-Dichlorobenzene	53°
p-Chlorobromobenzene	65°
Naphthalene	80°

All these solvents were very carefully distilled, and in addition the *p*-

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[1] This Journal, 39, 1662 (1917).

[2] Schlenk and Renning (*Ann.*, 394, 194 (1912)), have determined the molecular weight of diphenyl-α-naphthylmethyl in benzene by the cryoscopic method, obtaining values of 363 and 372 with concentrations of 2.4% and 2.8%, respectively. But we were unable to obtain even a 2% concentration of the free radical in benzene at the temperature of its freezing point, 6°.

dichlorobenzene and *p*-chlorobromobenzene were crystallized from alcohol.

The molecular depression constant of each solvent was determined for this particular apparatus and under exactly the same conditions that were to prevail in the experiments to follow, using as the solute triphenyl methane which had been painstakingly purified by repeated crystallization from alcohol and benzene. No correction was applied to the weight of the solvent to account for the amount which solidifies due to the supercooling and thereby decreases the actual quantity of material functioning as a solvent. For the supercooling was fairly uniform as a rule, and consequently this error is automatically taken care of to a large extent by the molecular depression constant of the solvent which was determined with approximately the same degree of supercooling.

The samples used for molecular-weight determinations were dried carefully in the manner previously described, and in addition, were heated under reduced pressure in a slow stream of carbon dioxide for one hour at a temperature of 50 to 60°, to insure the removal of all traces of solvent. As a rule, 3 additions were made which provided concentrations ranging from 1% to 3-4%.

Determination of the Molecular Depression Constants with $(C_6H_5)_3CH$ (244.1).

Solvent.	Solvent G	Triphenyl methane G	Concentration %	Depression of freezing point	Constant.
1 Nitrobenzene........ ..	23.39	0.2175	0.93	0.273	71.7
	..	0.4262	1.82	0.530	71.0
	..	0.6349	2.71	0.782	70.3
				Av.,	71.0
2 *p*-Bromotoluene..........	26.54	0.2817	1.06	0.366	84.2
	...	0.5238	1.97	0.680	84.1
	..	0.7826	2.95	1.013	83.9
				Av.,	84.1
3 *p*-Dichlorobenzene...... ...	19.86	0.2308	1.16	0.372	78.1
	...	0.4721	2.38	0.741	76.1
	...	0.7151	3.60	1.106	75.0
				Av.,	76.4
4 *p*-Chlorobromobenzene.....	24.60	0.2889	1.17	0.486	101.0
	...	0.6033	2.45	1.003	99.8
	...	0.9213	3.75	1.519	99.0
				Av.,	99.9
5 Naphthalene.............	17.66	0.2706	1.53	0.446	71.1
	...	0.5408	3.06	0.889	70.9
	...	0.8077	4.57	1.320	70.5
				Av.,	70.8

DETERMINATION OF THE MOLECULAR WEIGHT OF DIPHENYL-α-NAPHTHYLMETHYL.

Solvent	F p	Solvent G	Diphenyl naphthyl methyl G	Concentration %	Depression of freezing point	Molecular weight
1 Nitrobenzene	6°	23 23	0 2136	0 92	0 195	334 8
			0 4136	1 78	0 369	342 6
			0 6298	2 71	0 552	348 7
		24 00	0 2150	0 90	0 194	327 9
			0 4229	1 76	0 368	340 0
			0 6424	2 68	0 542	350 6
		23 41	0 2179	0 93	0 201	328 8
			0 4247	1 81	0 373	345 3
			0 6297	2 69	0 540	353 7
2 *p*-Bromotoluene	27°	26 56	0 2367	0 89	0 245	305 9
			0 5084	1 91	0 487	330 6
			0 7869	2 96	0 736	338 5
		26 48	0 2485	0 94	0 257	307 1
			0 4992	1 89	0 483	328 2
			0 7327	2 77	0 692	336 3
		26 71	0 2645	0 99	0 264	315 5
			0 5075	1 90	0 482	331 5
			0 7400	2 77	0 686	339 7
3 *p*-Dichlorobenzene	53°	20 01	0 2209	1 10	0 292	288 8
			0 4672	2 33	0 582	306 5
			0 7217	3 61	0 862	319 7
		19 90	0 2326	1 17	0 308	289 9
			0 4876	2 45	0 603	310 4
			0 7423	3 73	0 878	324 6
		19 89	0 2313	1 16	0 313	283 9
			0 4623	2 32	0 578	307 2
			0 7198	3 62	0 854	323 7
4 *p*-Chlorobromobenzene	65°	24 51	0 2748	1 12	0 410	273 2
			0 6025	2 46	0 827	296 9
			0 9520	3 88	1 257	308 7
		24 72	0 2665	1 08	0 397	271 3
			0 6116	2 47	0 839	294 6
			0 9626	3 89	1 263	308 0
		24 66	0 2915	1 18	0 423	279 2
			0 6178	2 51	0 836	299 4
			0 9577	3 88	1 241	312 6
5 Naphthalene[1]	80°	17 88	0 2175	1 22	0 336	256 3
			0 4445	2 49	0 667	263 9
			0 7125	3 98	1 035	272 6
		18 06	0 2136	1 18	0 329	254 5
			0 4402	2 44	0 649	265 9
			0 7073	3 92	1 016	272 9
		17 96	0 1976	1 10	0 304	256 2
			0 4387	2 44	0 655	264 0
			0 6982	3 89	1 011	272 2

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[1] THIS JOURNAL, 39, 1670 (1917)

Successive determinations showed that the freezing point of the solution of any definite concentration remained perfectly constant. This shows that no decomposition was taking place, and together with the fact that no hydrogen was being absorbed, is sufficient proof that no reduction of the free radical to diphenylnaphthyl methane was occurring in virtue of the possible catalytic effect of the platinum stirrer. As a further check, at the end of the experiment ether was added to the solution and air passed through it. From 80–82% of the peroxide was obtained instead of the usual 86%, offering in this way conclusive evidence that the free radical undergoes no change during the molecular-weight determination. In the following table, each experiment represents an individual preparation, and thus in no case were two determinations of the molecular weight made upon the same sample. Also, the sample was never more than one day old, the free radical being prepared in the afternoon, allowed to crystallize overnight, isolated the following morning and the molecular weight taken the same afternoon.

In the following diagram the results of the molecular-weight determinations are plotted in the form of curves, using the concentrations as abscissas and the values of the molecular weight as ordinates. (The molecular weight calculated for $(C_6H_5)_2(C_{10}H_7)C$ is 293.)

4. Discussion of Results.

Solutions of diphenyl-α-naphthylmethyl possess intense color, much more so than those of triphenylmethyl, but in the solid state both free radicals are almost wholly devoid of color. Attention has been called in a previous paper, and it is emphasized again, that in the opinion of the writers, "Not dissociation alone into triarylmethyl, but, in addition, the consequent tautomerization of this into its quinonoid modification constitute a satisfactory explanation of the color phenomena."

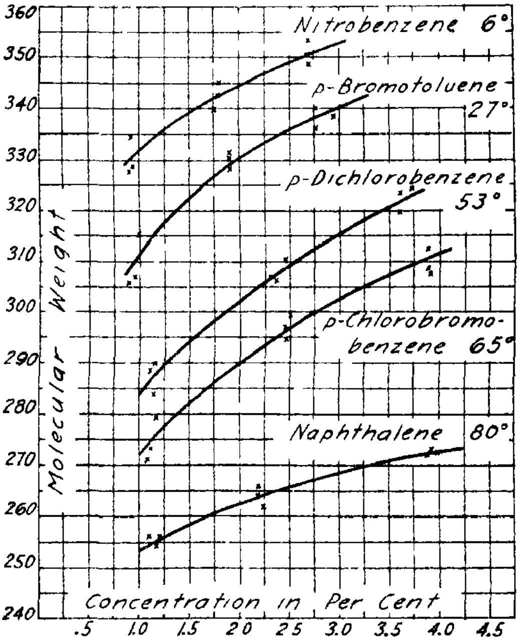


Fig 1.

The oxidation of diphenylnaphthylmethyl is similar in every respect to the oxidation of triphenylmethyl. In both instances there is equally rapid absorption and the theoretical amount of oxygen required to form the peroxide is absorbed, and in each case, approximately the same empirical peroxide factor of 86% is obtained.

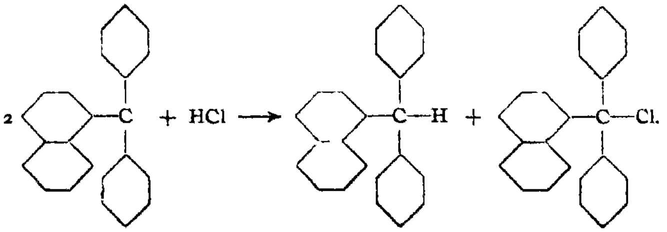
With iodine, diphenylnaphthylmethyl, like triphenylmethyl, reacts to form the corresponding iodide. But if the absorption of iodine is a measure of the degree of unsaturation, *i. e.*, the degree of dissociation into the monomolecular state, then the titration of the free radical to the iodide should proceed more nearly to completion with diphenylnaphthylmethyl than with triphenylmethyl. In reality, however, an equilibrium is reached when only 60% of the diphenylnaphthylmethyl has been transformed into the iodide, while the equilibrium with triphenylmethyl is not reached until 80% of the free radical has been titrated. It is evident that although the absorption of iodine shows the presence of a free radical, it does not serve as an indication of the extent to which the free radical exists in the monomolecular state. The reaction is more complex than one of simple addition between the free radical and iodine, as it involves a mobile equilibrium between the dimolecular and the monomolecular phases of the free radical as well as a mobile equilibrium between the monomolecular free radical and the resulting iodide, the limiting values of the latter equilibrium depending primarily upon the stability of the iodide and its tendency to dissociate.

$$R_3C - CR_3 \rightleftarrows 2R_3C.$$

$$R_3C + I \rightleftarrows R_3CI.$$

The action of hydrochloric acid upon a solution of diphenylnaphthylmethyl confirms in a measure the explanation advanced by Chichibabin to account for the production of *p*-benzohydryltetraphenyl methane by the action of hydrochloric acid upon triphenylmethyl. Two reactions take place simultaneously.

Triphenylmethyl reacts largely to form the polymer, *p*-benzohydryltetraphenyl methane, but 6% of triphenyl methane and triphenylmethyl chloride being formed; with diphenylnaphthylmethyl, however, the opposite is true, for in this case over 80% of the free radical goes to form diphenylnaphthyl methane and diphenylnaphthylmethyl chloride, the



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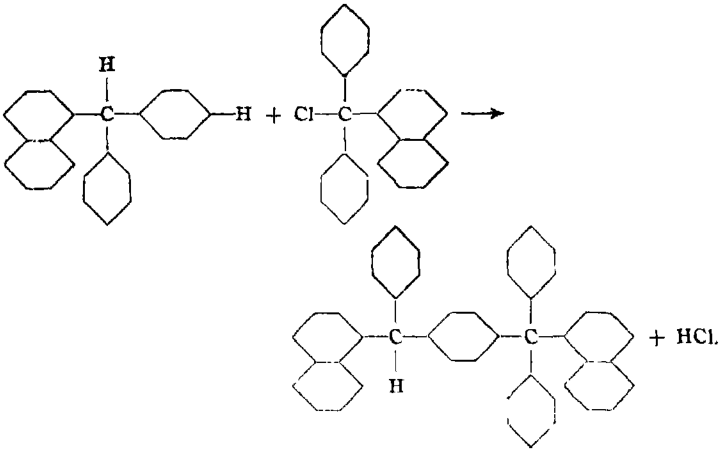
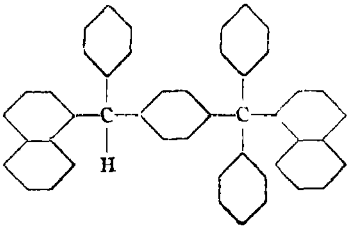
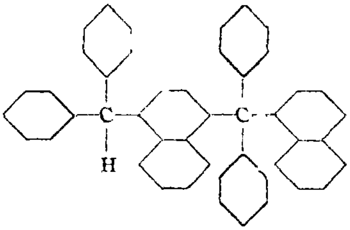


(2)

remainder condensing to give the polymer. This polymer, which is perfectly stable and agrees in its properties with *p*-benzohydryltetraphenyl methane, must be assigned one of two structures,



or



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The experiments concerning the formation of additive compounds with diphenylnaphthylmethyl lead to results which may seem at first to be wholly unexpected: namely, no addition is found to take place between this compound and the various classes of solvents. Therefore, the commonly accepted view that triphenylmethyl forms additive compounds solely in virtue of its tendency to exist partially in the monomolecular state must be abandoned. For if this were the case we should also have additive compounds with diphenylnaphthylmethyl, and, moreover, to a much greater extent than with triphenylmethyl.

How then can this apparent contradiction be explained? Unquestionably the typical, characteristic reactions of the triarylmethyls, such as oxidation and iodine absorption, are conditioned upon the existence of the equilibrium $R_3C — CR_3 \rightleftarrows 2R_3C$. But it need not necessarily follow that the more the R_3C phase is favored, the greater must be the reactivity of the compound in question. Indeed, on purely *a priori* grounds the very opposite view may be taken with equal force, and this view would apply particularly to such reactions of triarylmethyls as are readily reversible.

Consider for instance the case of triphenylmethyl itself. Hexaphenyl ethane constitutes a system which is on the border line between such ethane compounds wherein the central carbon atoms function as tetravalent and those wherein they function as trivalent. At room temperature the dissociation is only about 2 to 5% at most, but increases on warming and at 80° becomes appreciable, reaching as high as 25 to 30%. Being an unstable system, when chances for the formation of stable irreversible combinations with other compounds are lacking, triphenylmethyl will evidence its unsaturation through temporary, feeble attachment of one radical to another, or through attachment to substances such as ethers, aldehydes, ketones, esters, chloroform, carbon disulfide, and even to completely saturated substances like heptane. But all such combinations, whether it be free radical to free radical or free radical to something else, exist in virtue of the residual, though very feeble, affinity in triphenylmethyl. On the addition to the system of slight amount of energy from outside, as on gentle heating, the union is disrupted and the free radical regenerated. Thus, the obvious predilection of triphenylmethyl to assume the dimolecular state, and its proneness to enter into feeble combination with all possible solvents may be looked upon as consequences of one and the same cause, namely, that the trivalence of the carbon in triphenylmethyl is of a low order of stability. And now consider from the same point of view the case of diphenylnaphthylmethyl. It is monomolecular to the extent of 70% even at 6°; the dissociation increases with the temperature and reaches completion at 60°. Evidently, in this particular free radical the trivalence of carbon is of such high order of stability that the radical lacks the tendency to enter into combination with itself, and presumably for the very same reason it is devoid of tendency to unite with ethers, esters, ketones, etc. Or, if union does occur, it apparently is of such feeble nature that complete dissociation takes place at room temperature. Even in cases where the new compound results from the radical not in virtue of some undefined additional or potential valences but in virtue of definite chemical reaction, the combination may still prove one that is readily reversible, as for instance diphenylnaphthylmethyl iodide, wherein the equilibrium at room temperature is R_3CI 60%, R_3C 40%.

The above considerations lead to this conclusion: the higher the spontaneous dissociation of the hexa-aryl ethane, the greater the comparative stability of the corresponding triarylmethyl is likely to be. It is to be expected that the existence of the monomolecular phase preponderatingly over the dimolecular should be associated with a lack of propensity in the free radical to make additive compounds of the nature which characterize triphenylmethyl. This deduction is derived from the comparison of only two examples, and in the very nature of the case is only tentative. An examination of a large number of free radicals with this end in view is desirable.

It is not intended to convey the impression that the capacity of the hexa-aryl ethanes to form additive compounds is believed to be contingent entirely upon their dissociation. Undoubtedly other factors must be taken into consideration, such as the chemical nature of the individual free radical. Triphenylmethyl forms additive compounds with various solvents for the same reason in part that triphenyl methane itself forms additive compounds with benzene and other solvents. The unsaturation state of triphenylmethyl may greatly enhance its additive properties but it could hardly be considered as the sole factor in the formation of these compounds.

The results of the molecular-weight determinations of diphenylnaphthylmethyl in nitrobenzene, *p*-bromotoluene, *p*-dichlorobenzene, *p*-chlorobromobenzene, and naphthalene prove conclusively that we are dealing here with a phenomenon of molecular dissociation, wherein the products of dissociation are in equilibrium with the dissociating substance. An equilibrium of this nature might be expected to shift in favor of dissociation (1) with dilution, (2) with an increase in temperature.

(1) In every case, regardless of the nature of the solvent, we find that there is a steady increase in the molecular weight as we proceed from a 1% to a 3-4% solution of diphenylnaphthylmethyl, *i. e.*, an increase in concentration shifts the equilibrium in favor of the dimolecular modification and, *vice versa*, a decrease in concentration shifts the equilbrium in favor of the monomolecular modification. Moreover, it is evident from the similarity of the molecular-weight curves, Fig. 1, that this increase in dissociation with dilution is practically independent of the nature of the solvent.

(2) Likewise, we see from Fig. 1 that there is a marked decrease in the molecular weight of diphenylnaphthylmethyl with an increase of temperature, showing that the equilibrium is shifted in favor of dissociation. Indeed, if we compare solutions of a definite concentration, *e. g.*, 2%, and plot the temperatures as abscissas and the corresponding values of the molecular weight as ordinates, we obtain a remarkably smooth curve, shown in Fig. 2. From this curve it is evident that the effect of temperature upon the dissociation becomes greater as we proceed to higher temperatures, for the decrease in molecular weight for a given increase in temperature is not constant but becomes noticeably larger. In other words, between 70 and 80° for example, a change of 1° in the temperature produces a considerably greater effect upon the dissociation than a change of 1° between 10° and 20°.

The smoothness and uniformity of this temperature-molecular weight curve indicates that for a given concentration, the equilibrium between the monomolecular and the dimolecular forms of diphenylnaphthylmethyl is dependent largely upon the temperature and not to any appreciable extent upon the nature of the solvent, for otherwise we should expect noticeable irregularities in the curve.

From Fig. 2 we find that for a 2% concentration the molecular weight of diphenylnaphthylmethyl is approximately 345 at a temperature of 6°; therefore at this temperature an equilibrium is established between 30% of the dimolecular and 70% of the monomolecular form of the free radical. As the temperature is increased, the molecular weight drops until at about 62° it reaches the value of 293, indicating that at this point all of the dimolecular modification has dissociated and only the monomolecular modification is present in the solution.

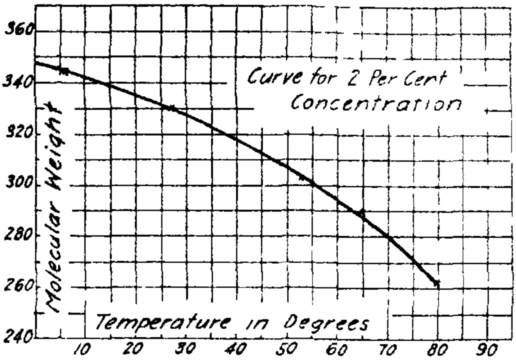

Fig 2

The molecular weight however does not become constant above this temperature but continues to decrease, reaching the value of 262 at 80.°. And indeed, other free radicals containing naphthyl groups seem to exhibit the same peculiar behavior, as for instance in the case of α-naphthylxanthyl[1] and α-naphthylphenyl(biphenyl)methyl.[2] How can these abnormal values be explained? The possibility arises that under the influence of comparatively high temperatures diphenylnaphthylmethyl may suffer a gradual decomposition of some sort. But any decomposition would necessarily be accompanied by a noticeable variation in the freezing point of the solution, and yet successive determinations showed that, on the contrary, the freezing point remained perfectly constant. Moreover such possibility of decomposition is precluded by the fact that by oxidizing the solution at the end of the experiment, the usual amount of peroxide could be obtained. In a previous contribution dealing with this phenomenon we ventured upon a hazardous explanation, namely that the triarylmethyl may suffer further dissociation with the consequent production of a radical with a bivalent carbon, as for instance:

$$(C_6H_5)_2C - C_{10}H_7 \rightleftarrows (C_6H_5)_2C + C_{10}H_7, \quad \text{or}$$

$$(C_6H_5)_2C - C_{10}H_7 \rightleftarrows (C_6H_5)C(C_{10}H_7) + C_6H_5$$

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[1] Gomberg and Schoepfle, THIS JOURNAL, 39, 1668 (1917).

[2] Schlenk and Renning, *Ann.*, 394, 195 (1912).

By reducing a solution of the free radical with hydrogen at a temperature of about 100°, and identifying the products formed, it was hoped that it would prove possible to determine whether such a dissociation of the monomolecular diphenylnaphthylmethyl occurs. But as in the case of reduction at ordinary temperatures, the reduced solution contained only diphenylnaphthyl methane so far as the examination revealed. Consequently the explanation suggested above still remains unsupported, and yet it seems difficult to find any other explanation equally satisfactory.

5. Summary.

(1) Several new diphenyl-α-naphthylmethyl derivatives have been synthesized and described.

(2) The important chemical reactions of the free radical, diphenyl-α-naphthylmethyl, have been studied including the oxidation, the reduction, the action of iodine, the action of light, and the action of hydrochloric acid.

(3) It has been shown that diphenyl-α-naphthylmethyl, unlike triphenylmethyl, does not form additive compounds with various solvents, in spite of its high degree of dissociation, and a plausible explanation for this difference has been suggested.

(4) By means of a series of exact molecular-weight determinations of diphenyl-α-naphthylmethyl extending over a range of temperature from 6° to 80°, it has been proven that the temperature as well as the concentration has a marked influence upon the degree of dissociation of free radicals, while the nature of the solvent seems to exert but slight influence.

(5) It has been shown that at a temperature of approximately 60° diphenyl-α-naphthylmethyl is present in the monomolecular phase entirely, and that above this temperature the molecular weight suffers a further decrease, the cause of which has not been established.

ANN ARBOR, MICH

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF COLUMBIA UNIVERSITY, No. 323.]

THE SYNTHESIS OF SOME HOMOLOGS OF THE TERPENES, DERIVATIVES OF 1,4-DIISOPROPYL CYCLOHEXANE.

BY MARSTON TAYLOR BOGERT AND CLARENCE PEAVY HARRIS.[1]

Received July 24, 1919.

Introductory Part.

An interesting fact concerning the terpenes, and one to which attention often has been called, is that the graphic formulas conventionally assigned to this numerous group of compounds all contain the following carbon skeleton, either as an open or as a closed chain·

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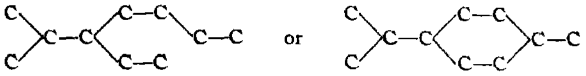
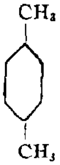
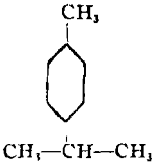
[1] The investigation reported in this article formed part of the work carried out by Mr. Harris as a candidate for the degree of Ph.D. under the Faculty of Pure Science, Columbia University. Its publication has been delayed by the war duties of the senior author.

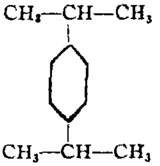


There is something peculiar about this arrangement of carbon atoms, the effect of which is to endow the compound with properties markedly divergent from the lower homologs of the same series, and this peculiarity of behavior seems to be referable to the isopropyl rather than to the methyl group.

The question presented itself therefore whether the presence of a second isopropyl group would cause any considerable change in properties as compared with homologs of the same series. The line of attack planned was to compare derivatives of the following types:


p-Xylene.


Cymene.


p-Diisopropyl benzene.

Derivatives of the first and second of these are numerous and well-known. Of the third type, very little appears to be on record.

As the hydrogenized hydrocarbons were regarded as most interesting, because of their structural relationship to the naturally occurring terpenes, the first problem was the synthesis and study of such substances, and this paper records the results so far accomplished in this direction. It is hoped to continue the investigation.

The only derivatives of 1,4-diisopropyl cyclohexane uncovered in our search of the literature were the *p*-diisopropyl cyclohexandiol-1,4 obtained by Wallach[1] on treating sabina ketone with methyl magnesium iodide, and the tetraphenyl *p*-phenylene glycol of Ullmann and Schlaepfer[2] prepared by the action of methyl magnesium iodide upon methyl terephthalate.

The new derivatives synthesized were as follows: tetramethyl *p*-phenylene glycol; 1,4-diisopropenyl benzene; 1,4-diisopropenyl-$\Delta^{1,4}$-dihydrobenzene; two isomeric $C_{12}H_{18}$ hydrocarbons from Δ^{1}-tetrahydroterephthalic acid; and certain bromine addition products of these hydrocarbons.

The synthesis of these compounds was carried out briefly as follows:

Cymene was oxidized to terephthalic acid by the action of sodium dichromate in presence of sulfuric acid, the terephthalic acid esterified, and the ester treated in anhydrous ether solution with methyl magnesium iodide, giving the glycol (I). This was then dehydrated by heating it with potassium hydrogen sulfate, yielding the diisopropenyl benzene (II).

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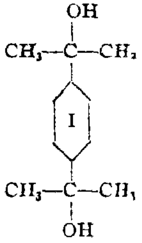
[1] *Ann.*, 263, 149 (1891); 302, 362 (1898).

[2] *Ber.*, 37, 2001 (1904).

In the case of the di- and tetra-hydrogenated compounds, obtained in similar manner from the hydrogenated terephthalic acids, the intermediate glycols (III and V) could not be isolated, as they lost water under the conditions of the experiment, passing immediately to the unsaturated hydrocarbons (IV, VI, VIII).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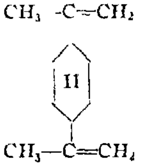
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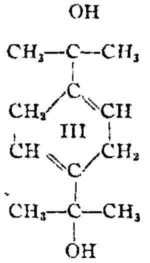
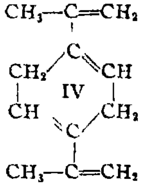
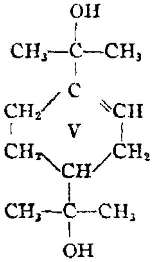

III


IV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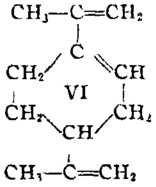
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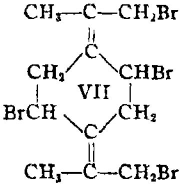
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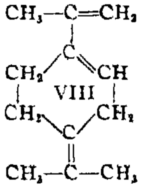
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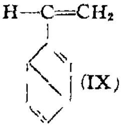
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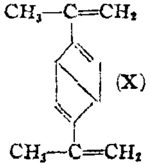
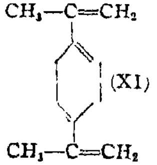

(X)


(XI)

Derivatives of II in general proved more stable and hence more readily isolated and purified than the corresponding derivatives of IV, VI or VIII.

Titration of II with a standardized solution of bromine in chloroform, and analysis of the product, both showed that 4 atoms of bromine had been added. Excess of the halogen caused no further addition nor any evolution of hydrogen bromide.

Hydrocarbon IV possesses a constitution resembling the $\Delta^{1,4}$-terpadienes, and, like the terpenes, gives a deep green coloration with acetic anhydride and sulfuric acid. It reduces permanganate in the cold, adds bromine and hydrogen bromide, and forms both a solid and a liquid tetrabromide like limonene, to which latter it is also related structurally. Treated with bromine in excess, it appears to take up but 4 atoms of bromine, after which substitution sets in, as evidenced by the evolution of hydrogen bromide. This corresponds with the results observed by Perkin in the case of the analogously constituted $\Delta^{3,8(9)}$-*p*-menthadiene, and was ascribed by him to the presence of a true conjugated system of double bonds. The structure of the tetrabromide of IV therefore is probably that pictured in Formula VII; the solid and liquid forms being the *cis* and *trans* isomers.

Hydrocarbon VI (or VIII), obtained from tetrahydro terephthalic acid in two isomeric forms, was much more sensitive to the action of bromine than either II or IV. Although these isomers decolorized the bromine solution instantly when first added, elimination of hydrogen bromide began very soon and we were unable to control it or to separate any pure bromo derivative from the products, the latter being oily, viscous and intractable.

The behavior of the 4 hydrocarbons (II, IV, VI and VIII) towards bromine is thus quite different and obviously reflects some difference in their constitution. The smooth addition of 4 bromine atoms to II, the absence of any hydrogen bromide evolution even when excess of the halogen was employed, and the stability of the final product, all indicate side-chain and not nuclear addition. It is analogous to the addition of bromine to *p*-isopropenyl toluene[1] or to isopropenyl benzene.[2] On the other hand, Wallach[3] noted many years ago the evolution of hydrogen bromide during the formation of terpene tetrabromides, and Perkin[4] made a similar observation in the addition of bromine to certain *p*-menthadienes. Other investigators have had like experiences, and it is a well established fact that where bromine is attached to the carbon of a hydroaromatic nucleus hydrogen bromide splits out very easily. The indications therefore are that in the other unsaturated hydrocarbons (IV, VI and VIII) bromine adds to nuclear carbon and hydrogen bromide then splits out with formation of various as yet unidentified derivatives.

In the case of the $C_{12}H_{18}$ hydrocarbons prepared from tetrahydro terephthalic acid, it has not been determined as yet whether they represent the two possible structural isomers (VI and VIII) which can be formed from the dicarbinol by loss of water, or whether they are only geometrical isomers of one of these two (VI).

A discussion of the refractivities and magnetic rotatory powers of the new hydrocarbons will be found in the Experimental Part.

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[1] Perkin, *J. Chem. Soc.*, **87**, 654 (1905).

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[4] *J. Chem. Soc.*, **87**, 667, 1101, 1102 (1905).

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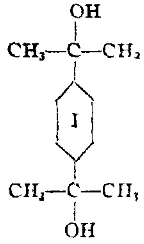

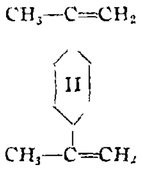

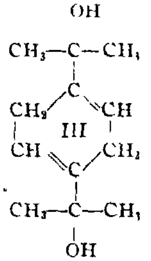

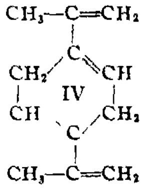

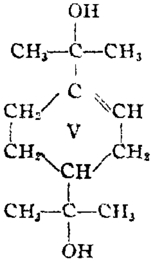

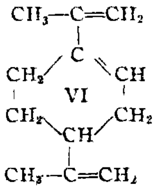

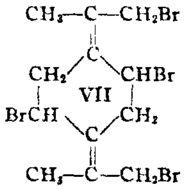

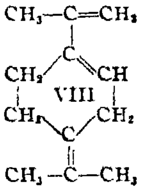

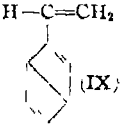

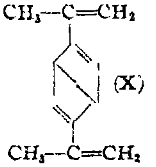

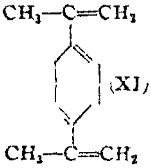

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[1] Perkin, *J. Chem. Soc.*, 87, 654 (1905).

[2] Perkin, *Ibid.*, 87, 672 (1905).

[3] *Ann.*, 279, 389 (1894).

[4] *J. Chem. Soc.*, 87, 667, 1101, 1102 (1905).

In the course of this study, an improved process for the production of terephthalic acid from cymene was developed; and the methods of Baeyer for the preparation of $\Delta^{1,4}$-dihydro- and Δ^{1}-tetrahydroterephthalic acids were modified as so to improve the yields considerably.

Experimental Part.

p-Di(hydroxyisopropyl) Benzene (1,4-Di(isopropanol-2) Benzene) (Formula I).—The raw material was crude cymene from the paper mills, which was washed with alkali, steam distilled and then fractioned under diminished pressure. In most cases, the distillation under reduced pressure could be dispensed with, the yields of terephthalic acid being just about as good when the dried steam-distilled product was used direct.

This cymene was oxidized by boiling it, under a return condenser, with a mixture of sodium dichromate and sulfuric acid. To a solution of 560 cc. of conc. (sp. gr. 1.84) sulfuric acid in 1500 cc. of water, 440 g. of technical sodium dichromate was added, and then 50 g. of cymene, and the whole boiled gently until the oxidation was completed, which was usually after about 48 hours boiling. It was found necessary to use resistance glass flasks, and to protect the corks with tinfoil against the solvent action of the cymene.

Upon completion of the oxidation, the mixture was diluted with an equal volume of water, the crude acid filtered out, washed thoroughly with water, dried at 110° to remove traces of cymene, and then washed again with water to remove small amounts of chromium salts not easily eliminated so long as any cymene is present. The product thus obtained was micro-crystalline and nearly colorless. This method of purification was found more satisfactory than solution in alkali and reprecipitation by acid. Final purification was always accomplished through the methyl ester. Yield of terephthalic acid by the above process, 25-28 g., or approximately 45% of the theoretical amount.

In spite of the slight solubility of both terephthalic acid and of its methyl ester in methyl alcohol, the acid when suspended in this solvent can be esterified in two or three hours by the action of dry hydrogen chloride. The course of the reaction can be followed by the change in the appearance of the suspended solid from the granular condition of the free acid to the needles or plates characteristic of the methyl ester. The ester so prepared was crystallized once from ethyl alcohol and was then quite pure, m. p. 140.8° (corr.). Yield, 80 g. of pure ester from 100 g. of crude acid, or about 70% of the theoretical amount.

By the action of methyl magnesium iodide upon methyl terephthalate, the desired dicarbinol was obtained.

This step presented something of a problem, owing to the very slight solubility of the ester in anhydrous ether. After experimenting with various methods and different forms of apparatus, the one described below, using the apparatus depicted in Fig. 1, was devised and proved the most satisfactory.

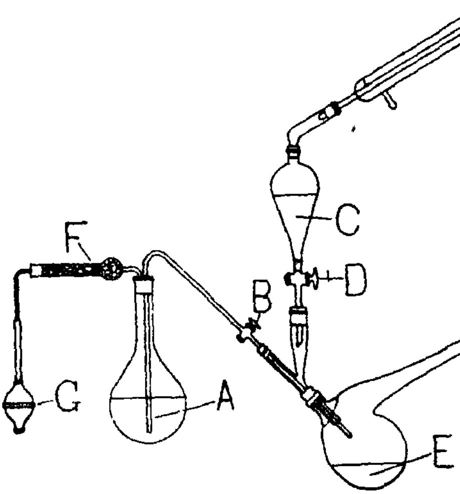

Fig 1

20 g. of methyl terephthalate was placed in the separatory funnel C. The Grignard reagent was prepared in the flask A from 10 g of magnesium, 60 g. of methyl iodide and 800 cc. of anhydrous ether. 200 cc. of anhydrous ether was introduced into the retort E and heated gently so that the ether distilled over into C at the rate of about 10 cc per minute, there dissolving the crystalline ester and carrying it down into E. As soon as this saturated solution of the ester began to enter the retort, a small amount of the Grignard reagent was blown over into the retort by compressing the bulb G. Instead of a rubber bulb, in later experiments there was employed a source of constant pressure, controlling the flow by the stopcock B. F contained soda-lime and calcium chloride. By this manner of operating, there was never any large excess of Grignard reagent in the reaction vessel E, and less danger of splitting water out of the tertiary alcohol formed.

The ester was dissolved completely in 3 or 4 hours, after which the contents of E were boiled gently for another hour, and then left over night at laboratory temperature. The ether was decanted from the insoluble addition product, the latter decomposed by ice and dil. hydrochloric acid, and the mixture warmed on the water bath to remove ether. The dicarbinol was then filtered off and washed with water to free it from magnesium salts. The somewhat sticky solid was heated at 100° for half an hour with 200 cc. of 5% aqueous caustic alkali solution, to eliminate traces of iodine and to saponify any unchanged methyl terephthalate, filtered, washed free from alkali, and crystallized twice from 50% ethyl alcohol. The dicarbinol was thus produced in colorless, short, lustreless needles; m. p. 142 4–142.9° (corr.), it was insoluble in water, but moderrately soluble in alcohol or in glacial acetic acid. The yield of crude product was 15 g., or 85% of the theoretical amount; of pure substance, 10 g., or 50% of the theoretical amount.

Calc. for $C_{12}H_{18}O_2$ C, 74 23, H, 9 28 Found· C, 74 0, 73 8; H, 9 5, 9 4.

1,4-Diisopropenyl Benzene (Formula II).—This diolefin was prepared from the above carbinol by heating it with dry powdered potassium hydrogen sulfate. As it polymerizes very readily, some investigation was necessary to ascertain the conditions requisite for good yields. The following procedure gave the best results:

8 g. of the dicarbinol was mixed intimately with 4 g. of powdered potassium hydrogen sulfate and distilled under reduced pressure, maintaining the temperature of the bath at 150° to 160°. At a pressure of 20 mm., the diolefin distilled over at 110 to 123°, condensing to a colorless highly refractive liquid which soon changed to a white solid. Yield, 4.5 g., or 68.4% of the theoretical amount.

This hydrocarbon crystallized from dil ethyl alcohol in micaceous plates with high nacreous lustre, and possessed a very pleasant odor. It was easily soluble in the ordinary organic solvents at their boiling points. Recrystallized to constant m. p., it melted at 63.6–64° (corr.).

Calc. for $C_{12}H_{14}$. C, 91.13, H, 8 87. Found. C, 90.8, 90 2; H, 8.7, 8.8
M W. calc., 158 Found 153

Tetrabromide.—Diisopropenyl benzene dissolved in chloroform was titrated with a standardized solution of bromine in the same solvent, determining the end-point with starch-iodide paper. The addition proceeded rapidly at first, but slowed up toward the close, making the exact reading of the end-point a matter of considerable difficulty. No evolution of hydrogen bromide was observed at any time during the reaction. The amount of standard solution consumed showed that the hydrocarbon had taken up 4 atoms of bromine.

Evaporation of the chloroform solution yielded a solid, together with a small amount of a liquid product. Recrystallization of the solid gave pale yellowish, cubical crystals, m. p. 130.3–131.3° (corr.), of impure tetrabromide. In spite of 3 further recrystallizations from ethyl acetate, the product remained impure; but the amount of bromine found on analysis indicated that it was evidently a tetra- and not a dibromide. Insufficient material prevented further work in this direction.

1,4-Diisopropenyl-$\Delta^{1,4}$-dihydrobenzene (Formula IV).—Baeyer[1] found that when terephthalic acid was reduced by sodium amalgam, the first product of the reduction was the $\Delta^{2,5}$-dihydro acid. Upon boiling this with water, the $\Delta^{1,5}$-dihydro acid was formed, whereas heating with alkali gave the $\Delta^{1,4}$-dihydro acid. The latter is therefore the most stable of the three and by carrying out the reduction at slightly elevated temperatures without neutralizing the alkali, the $\Delta^{1,4}$ acid was the main product

On repeating this work, we found that the yield of $\Delta^{1,4}$-dihydro acid could be materially increased by various modifications of Baeyer's original process, and the method finally adopted was as follows:

10 g. of methyl terephthalate was saponified by boiling with 500 cc. of water containing 5 g. of sodium hydroxide, the solution was cooled to 50°, diluted to a liter and reduced by successive additions of 100 g. portions of 3% sodium amalgam, with vigorous stirring, until the permanganate test[2] showed a faint cloud only. It is essential that all of the terephthalic acid be reduced at this point and before taking the next step in the process, since the solubilities of its ester are much the same as those of the methyl ester of the dihydro acid and the complete separation of the two is therefore a matter of no little difficulty. The mixture was heated an hour longer on the water bath, to complete the conversion of all $\Delta^{2,5}$ and $\Delta^{1,5}$ acids into the $\Delta^{1,4}$ isomer, the aqueous layer decanted from the mercury, nearly neutralized and filtered. The filtrate was made strongly acid with hydrochloric acid, the $\Delta^{1,4}$-dihydro acid filtered out, washed and dried. Yield, 6.3 g. of crude acid, or 73% of the theoretical amount.

10 g. of this crude $\Delta^{1,4}$-dihydro acid was converted into the acid chloride by heating with excess of phosphorus pentachloride. The crude chloride was cooled in a freezing mixture and, without further purification, cold methyl alcohol was added to it slowly. The ester separated almost immediately in small, white prisms. These were filtered out, washed with methyl alcohol, and recrystallized from ethyl alcohol, giving short, thick, lustreless prisms. From ethyl acetate, it crystallized in rhombs resembling calcium oxalate in appearance. Yield, 4.8 g., or 41% of the theoretical amount. M. p. 128.4–129.4° (corr.). Baeyer gives the m. p. as 130° uncorrected.

This dimethyl ester was treated with methyl magnesium iodide, in anhydrous ether solution, in exactly the same way as already described for methyl terephthalate, but no carbinol was isolated, dehydration occurring under the conditions of the experiments and the diolefin being the sole product recovered.

From 12 g. of the ester, 6.5 g. of magnesium and 38 g. of methyl iodide,

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[1] *Ann.*, **245**, 103 (1887); **251**, 272, 292 (1889); **256**, 1 (1890); **258**, 1, 145 (1890); **266**, 169 (1892); **269**, 169 (1892); see also Perkin, *J. Chem. Soc.*, **87**, 1083 (1906).

[2] Baeyer, *Ann.*, **245**, 147 (1888).

9.5 g. crude product, or 79% of the theoretical amount was obtained. Direct crystallization of this crude product from alcohol, or distillation under diminished pressure, followed by crystallization from alcohol, gave only the unsaturated hydrocarbon and no dicarbinol. The hydrocarbon separated from alcohol in plates, with faint nacreous lustre, difficultly soluble in water, but soluble in most of the ordinary organic solvents on heating. M. p. 117–117.5° (corr.).

Calc. for $C_{12}H_{16}$: C, 90.0, H, 10. Found C, 90.0, H, 10 1.
M. W calc, 160. Found 161 5

Tetrabromide.—When this hydrocarbon was dissolved in chloroform and titrated with a standardized solution of bromine in the same solvent, the bromine solution was decolorized until 1.93 moles, or approximately 4 atoms of the halogen had been taken up. At this point the yellow color of the solution remained and a small amount of hydrogen bromide was evolved. Evaporation of the chloroform solution yielded an oil which could not be handled.

By carrying out the addition of the calculated amount of bromine in glacial acetic solution, a small amount of cubical crystals was secured, which melted at 107 to 109° (corr.) after recrystallization from ethyl acetate. Only 0.13 g. of these crystals was recovered.

Calc for $C_{12}H_{16}Br_4$· Br, 66 7 Found· 67 4

Hydrocarbons from Δ^1-Tetrahydro Terephthalic Acid (Formulas VI and VIII).—Δ^1-Tetrahydro terephthalic acid was produced from terephthalic acid according to the method of Baeyer,[1] with a few modifications introduced to increase the yield. The amount of crude tetrahydro acid recovered averaged 96% of the theoretical quantity. The crude acid was converted into the acid chloride by the action of phosphorus pentachloride, and the chloride then changed to the methyl ester by the action of methyl alcohol at low temperature. The methyl alcohol solution of the ester so obtained was poured slowly into a saturated aqueous solution of sodium hydrogen carbonate, which caused the ester to separate on top of the solution as an oily layer which quickly solidified. This was collected with ether, the ethereal solution dried with calcium chloride and fractioned under reduced pressure, the ester coming over at 153.3 to 154.5° (corr.) at 20 mm. Yield, 45% of the theoretical amount. From water, it crystallized in colorless needles, m. p. 35.2–36.2° (corr.), soluble in most of the ordinary organic solvents.

When this ester was subjected to the action of methyl magnesium iodide, in dry ether solution, in the manner described above for the other esters, the dicarbinol was probably the main product of the reaction, because when it was distilled under diminished pressure, both water and unsaturated hydrocarbon were recovered. Attempts to isolate the carbinol from the crude product however proved fruitless, so it was heated for 15 minutes at 180 to 190° with excess of potassium hydrogen sulfate, water added, the mass extracted with ether, the ethereal solution separated, dried over solid sodium hydroxide, decanted, the ether removed by distillation, and the residue fractioned at 20 mm. pressure.

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[1] *Loc. cit.*

From 9 g. of crude carbinol, there were obtained 5 g. of a fraction (A), b. p. 95–98° at 20 mm., and 3 g. of a fraction (B), b. p. 105–108° at the same pressure Both were colorless oils, and on analysis proved to be isomeric $C_{12}H_{18}$ hydrocarbons.

Analysis of A Calc for $C_{12}H_{18}$ C, 88.9, H, 11.1 Found C, 88.5; H, 10.98. M W calc, 162 Found 164.

Analysis of B Calc for $C_{12}H_{18}$ C, 88.9, H, 11.1 Found C, 88.8, H, 10.95. M W calc, 162 Found 154

Upon long standing in the air, both isomers became viscous and slightly yellow.

Towards bromine, the behavior of the two isomers was much the same. Various solvents were tried. The bromine was absorbed quickly at the outset, but very soon evolution of hydrogen bromide began and the yellow color of the solution disappeared but slowly Addition of bromine therefore was continued as long as any reaction was evident, but the products were thick oils, from which no pure bromine dervatives could be separated.

Specific Gravities, Refractivities, and Magnetic Rotatory Powers of the New Hydrocarbons.

Specific Gravity.—The density of the liquid hydrocarbons ($C_{12}H_{18}$) was ascertained by use of a 1 cc. pycnometer. In the case of the solids ($C_{12}H_{14}$ and $C_{12}H_{16}$), the specific gravity was determined by the "free-swimming" method regarded by Nernst[1] as the most accurate for small quantities of material. We employed the modification recommended

TABLE I.

Specific Gravities.

Liquid	Substance	Per cent	Solvent	Specific gravity.	Temp T_4.
1.	(a)			1.0649	22.3
2	(a)	5.11	Benzene	0.8843	16.0
3	(a)	4.27	Chloroform	1.4547	19.0
4	(b)			1.0669	20.0
5	(b)	3.76	Benzene	0.8836	16.0
6	(b)	4.79	Chloroform	1.4447	16.0
7	$(c)^{96}$	..	..	0.8715	20.0
8	$(c)^{106}$			0.8706	20.0
9			Benzene	0.8832	17.5
10	..		Chloroform	1.4939	15.8
11	(b)	3.19	Benzene	0.8853	15.0
12	(a)	4.57	Benzene	0.8872	15.0

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[1] *Theoretical Chemistry*, from 6th German ed., 1911, p. 305.

by Andrae.[1] The density of solutions of these solids was determined with a Westphal balance, and chloroform and benzene were used as the solvents.

Table I gives the results of these determinations, the concentration of solute, density of solvent, and temperature (referred to water at 4°).

In this and the following tables, (a) = $C_{12}H_{14}$, (b) = $C_{12}H_{16}$, and (c) = $C_{12}H_{18}$; $(c)^{95}$ being the fraction boiling at 95–98° at 20 mm., and $(c)^{105}$ being the fraction boiling at 105 to 108° at same pressure.

Refractivity.—The determination of the refractive powers of these hydrocarbons was found somewhat troublesome, because of their slight solubility at the temperature employed, and the relatively high m. p. of the $C_{12}H_{16}$ compound. It was necessary therefore to use quite dilute (3% to 5%) solutions.

The coefficients of refractivity were determined by means of the Pulfrich refractometer, using a Geissler hydrogen tube as the source of illumination. The indices of refraction were found in all cases for the α hydrogen or C line, and where chloroform solutions were used were determined also for the γ hydrogen or G line.

Molecular refractivities (*M*) were calculated by both the Gladstone-Dale (Table III) and the Lorentz-Lorenz (Table II) formulas. The admixture formulas, as given by Eisenlohr[2] were employed. According to Smiles[3] the admixture formula is accurate "if the solvent and solute have nearly the same refractive index; but if these differ much from one another" the results are not so reliable. Two solvents, benzene and chloroform, therefore were employed and the average result taken as the nearest approximation to the truth.

In Tables II and IV (Lorentz-Lorenz formula), and III (Gladstone-Dale formula), the liquids listed in the first column are the same as those given in Table I. Not much reliance should be placed upon Table IV, as the violet hydrogen line was indistinct in the instrument used; and for this reason the dispersivities were not calculated.

Molecular refractivities were calculated from the atomic values recently revised by Eisenlohr;[4] figuring, for compound II, 12 C, 14 H and 5 double bonds; for compound IV, 12 C, 16 H and 4 double bonds; and for compounds VI and VIII, 12 C, 18 H and 3 double bonds.

To reduce the errors and inaccuracies arising from the determination of molecular refractivities in such dilute solutions, and to get a nearer approach to the truth, the average values obtained by the use of two solvents, benzene and chloroform, differing considerably from each other in refractive index, were calculated and appear in Table V. These were figured from Table II, since the Lorentz Lorenz formula is believed to give results more nearly correct than the Gladstone-Dale expression.

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[1] *Z. physik. Chem.*, 76, 491 (1911).

[2] *Spektrochemie organischer Verbindungen*, Stuttgart, 1912, p. 189.

[3] *Chemical Constitution and Physical Properties*, London, 1912, p. 244.

[4] *Z. physik. Chem.*, 75, 585 (1910).

TABLE II

Liquid	Index H_α or C	n^2-Form Spec ref	n^2 Form M(calc)	M(obs)	Exaltation
2	1 49755	0 35868	52 674	56 687	4 013
3	1 44985	0 35660	52 674	56 343	3 669
5	1 49593	0 35167	53 171	56 267	3 095
6	1 45005	0 36475	53 172	57 629	4 458
7	1 48717	0 33013	53 670	53 481	—0 189
8	1 48650	0 33080	53 670	53 473	—0 197
9	1 49421				
10	1 44172				

TABLE III

Liquid	Index H_α or C	n Form Spec ref	n Formula M(calc)	M(obs)	Exaltation
2	1 49755	0 61965	90 2	98 01	7 81
3	1 44985	0 61320	90 2	96 95	6 75
5	1 49593	0 60398	90 4	96 71	6 31
6	1 45005	0 62642	90 4	100 31	9 91
7	1 48717	0 55902	90 6	90 64	0 04
8	1 48650	0 55883	90 6	90 61	0 01

TABLE IV

Liquid	Index H_γ or G′	n^2 Form Spec ref	n^2 Formula M(calc)	M(obs)	Exaltation
3	1 46620	0 36192	54 765	57 184	2 419
6	1 46570	0 36591	55 112	58 546	3 434
7	1 50902	0 34264	55 457	55 508	0 051
9	1 52082				
10	1 45852				

TABLE V

Substance	M(calc)	M(observed)	Exaltation
(a)	52 674	56 515	3 841
(b)	53 172	56 948	3 776
(c)^{35}	53 670	53 481	—0 189
(c)^{106}	53 670	53 473	—0 197

Examination of Table V discloses the fact that the difference in exaltation between compounds (a) and (b) is within experimental error. If the structures assigned to these two hydrocarbons are correct, they differ only in that one contains a true benzene nucleus and the other a dihydrobenzene nucleus. The exaltation observed in the case of compound (b) is assumed to be due to the presence of two systems of conjugated double bonds. The exaltation recorded for compound (a) therefore would indicate the existence in it also of two such systems of double bonds, an assumption which is in line with the exaltation characteristic of styrene and of other benzenoid compounds having an unsaturation adjacent to the nucleus, a fact which has been explained on the hypothesis that the external double bond becomes conjugated with an adjoining unsaturation of the nucleus. The third unsaturation occurring in the nucleus of (a) must bear a somewhat different relation to the molecule, or there would be 5 sets of conjugated double bonds present and a correspondingly higher refractivity.

It is perhaps of interest to point out here that the Dewar formula for styrene (IX) contains but one system of conjugated double bonds and should therefore exhibit a smaller exaltation than hexatriene, and this has been found to be the fact. On the same formulation, diisopropenyl benzene (X) shows but two such systems and the same is true of its dihydro derivative (XI). The difference in refractive power between the two therefore would be that due solely to the *para* bond. If we regard the centric formula for benzene as nearest the truth, we may look upon the Dewar formulation as the phase in which this centric formula preferably presents itself in the case of styrene and related compounds. The fact that the first reduction product of terephthalic acid is the $\Delta^{2,5}$-dihydro acid apparently links it up with this *para* bond relation also.

That the $C_{12}H_{18}$ hydrocarbons gave a slight depression instead of an exaltation in molecular refractivity seems at first sight rather puzzling, in view of the assumed presence in their molecules of a conjugated system of double bonds, but the case is not unique, as it falls exactly into line with $\Delta^{1,3}$-dihydrobenzene, which both Harries[1] and Willstatter[2] found to give normal and not exalted values for refractivity.

Magnetic Rotatory Power.—The apparatus employed consisted of an electromagnet having a hollow core to permit the passage of light, and with a polariscope attached to the same frame. The compound to be examined was placed in a 5 cm. tube between the poles, and the same tube was used in all the experiments, so as to avoid errors due to variations in the thickness of the liquid. The angle was read to hundredths of a degree, and conductivity water was taken as the standard.

Table VI gives the angle readings with direct and reversed currents, the total rotation, specific rotation, calculated and observed molecular rotation, and magneto-rotatory exaltation. The molecular rotatory power was calculated by the usual formulas for a pure liquid and for a solution.

Table VII shows the average of the results with two different solvents, benzene and chloroform. The liquids used in Tables VI and VII, appearing in the first column, are the same as those given in Table I.

[1] *Ber.*, 45, 809 (1912).

[2] *Ibid.*, 45, 1468 (1912).

TABLE VI.

Liquid	Rotation Direct	Rotation Reversed	Total	Spec rot	*M*(calc)	*M*(obs)	Exaltation
Water	4.40	−1.19	5.59				
3.	5.11	−1.81	6.92	2.962	13.501	24.404	10.903
12	7.16	−3.86	11.02	2.671	13.501	22.003	8.502
6	4.88	−1.73	6.61	2.028	13.256	16.753	3.497
11	7.09	−3.86	10.95	2.019	13.256	16.649	3.393
7	5.79	−2.79	8.58	1.535	13.011	15.852	2.841
8	5.82	−3.06	8.88	1.588	13.011	16.423	3.412
9	4.86	−1.54	6.40				
10	7.16	−3.77	10.93				

TABLE VII

Substance	Spec rot	*M*(calc)	*M*(obs)	Exaltation
(a)	2.817	13.501	23.204	9.703
(b)	2.024	13.256	16.701	3.445
(c)	1.562	13.011	16.137	3.126

In considering the results obtained by magnetic rotation, it may be recalled that Perkin[1] found the difference in magnetic rotation between cyclohexane and benzene, 5.62, to be almost identical with that observed between hexane and hexatriene, 5.55, and concluded that benzene contained 3 conjugated systems of double bonds. By a comparison of the rotations of limonene and the isomeric $\Delta^{3,8(9)}$-*p*-menthadiene, he deduced the value of the conjugation as 1.82.

A glance at Table VII shows a value of 9.7 for *p*-diisopropenyl benzene, or the equivalent of 5 conjugated systems of double bonds (5 × 1.82 = 9.1), a result which must be explained on the assumption that, in the magnetic field at least, this hydrocarbon possesses a nucleus corresponding to a Kekulé and not to a Dewar formula.

Diisopropenyl dihydrobenzene contains two conjugated systems of double bonds and should accordingly show a rotation of 2 × 1.82 = 3.64, which is very close to the value of 3.45 actually found.

The behavior of the tetrahydro derivatives (c) is analogous to that of $\Delta^{1,3}$-dihydrobenzene, which shows a normal refractivity but a magnetic rotatory exaltation,[2] although the figure actually found, 3.1, is somewhat higher than it should be for the structures assigned.

Recapitulating the observations noted in the foregoing concerning these new hydrocarbons:

Compound a (Formula II, $C_{12}H_{14}$) towards bromine gives no evidence of the presence of any conjugated systems of double bonds, but adds 4 bromines like a simple diolefin. Its molecular refractivity, on the other hand, indicates the presence of two such systems; and, in the magnetic field, it behaves as though possessing 5 such systems.

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[1] *J. Chem. Soc.*, **69**, 1025 (1896), **91**, 810 (1907).

[2] Perkin, *J. Chem. Soc.*, **89**, 854 (1906); **91**, 806 (1907).

Compound b (Formula IV, $C_{12}H_{16}$), in its behavior with bromine, its molecular refractivity and its magnetic rotatory power, acts consistently as though containing two systems of conjugated double bonds.

Compounds c (Formulas VI and VIII, $C_{12}H_{18}$) act towards bromine like substances containing conjugated double bonds such as to cause nuclear addition and not simple addition to side chains, although no pure bromine derivatives could be isolated. In their molecular refractivities and magnetic rotatory powers, they resemble $\Delta^{1,3}$-dihydrobenzene.

A dynamic representation of benzenoid structure, similar to that proposed by Collie,[1] which includes different static formulas as phases of its vibration, lends itself best to the interpretation of the behavior of the hydrocarbons described above.

Summary.

1. Unsaturated hydrocarbons, related to the terpenes, have been prepared by the action of methyl magnesium iodide upon methyl terephthalate and its di- and tetrahydro derivatives.

2. The new compounds prepared were the 1,4-diisopropenyl benzene ($C_{12}H_{14}$); 1,4-diisopropenyl-$\Delta^{1,4}$-dihydrobenzene ($C_{12}H_{16}$); 1,4-diisopropenyl-Δ^{1}-tetrahydrobenzene ($C_{12}H_{18}$), or an isomer thereof; tetramethyl *p*-phenylene glycol; and certain bromine addition products of the new hydrocarbons.

3. The refractivities and magnetic rotatory powers of the new hydrocarbons, as well as their densities, have been determined and are discussed with reference to their bearing upon the structures assigned to these compounds.

NEW YORK CITY

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF CASE SCHOOL OF APPLIED SCIENCE.]

THE GENESIS OF PETROLEUM AS REVEALED BY ITS NITROGEN CONSTITUENTS.

BY CHARLES F. MABERY.

Received July 26, 1919.

From what is known concerning natural processes of building up complex nitrogen organic compounds they are limited to the agency of vegetable or animal life. The circuitous laboratory methods leading through many changes to intricate structure have no counterpart in nature except through the influence of the life principle. If, therefore, such nitrogen derivatives are universally present in petroleum it is difficult to avoid the conviction that these bodies had their origin as evolution products of organic life, and that the hydrocarbons with which they are associated were evolved from the same source. The universal presence of nitrogen compounds thus becomes of considerable interest as a determining feature of the genesis of petroleum especially since several of the heavier varieties, notably those from the California and Russian fields have been found to contain nitrogen compounds in large proportions. In a wide area of the California fields sufficient organic débris has been disclosed to account for all the oil in that region. The great deposits of petroleum here are unique in their conformation, and in respect to the nature of the oil are most interesting from the point of view of its composition. Like the immense stores in the Trenton Limestone of Ohio and Indiana the residual material from which it was formed is close at hand. Recent discoveries in California by Dr. Dickinson, of the "Martinez" beds of the Iocene period has revealed in a broad expanse of marine shell life, 4000 feet thick, an abundant supply of organic material for the origin of all the oil in those great fields. In view of the immense production of petroleum in Russia, chiefly at Baku and Bibi-Eibat, it is surprising that the Russian government has made no investigation of its origin nor of the geological conditions of its formation. Were it not for the assiduous labor of Mr. A. Beeby Thompson who spent several years in those oil fields as an engineer in the interests of European promotors nothing would be known concerning them. The results of his observations are published in a book entitled "The Oil Fields of Russia," London, 1904. In describing the oil sands and associated rock strata, Thompson denies an inorganic origin for Russian oil; vegetable matter he regards as doubtful, but animal or marine remains as the more probable source.

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[1] *J. Chem. Soc.*, **71**, 1013 (1897).

Of the numerous speculative suggestions relating to the genesis of petroleum, its formation from carbides in the hot regions of the earth's interior is perhaps the most plausible, for in the laboratory through acetylene hydrocarbons may be synthesized from metallic carbides. Assuming, however, such questionable formation of carbides, and the subsequent synthesis of petroleum hydrocarbons, it is scarcely conceivable that those hydrocarbons could withstand intimate contact with other volcanic vapors, nor the intense heat of volcanic conditions which has been suggested as the means of their transference to the geologic strata where petroleum is found. Still less could the unstable nitrogen derivatives of these hydrocarbons, if their similar synthesis could be imagined, survive exposure to such destructive conditions. The only possible source of these bodies was organic matter imbedded in the rock strata, and their solution in petroleum if formed from carbides could have resulted only from contact with infiltrated liquid hydrocarbons.

The heavier varieties of petroleum in the California, Texas, Ohio, Canada, Russian and similar fields, are complex mixtures of the denser hydrocarbons with oxygen, sulfur and nitrogen derivatives. They all differ widely in composition from the lighter varieties in the Eastern territory of the

United States, Pennsylvania, W. Virginia and the Berea Grit of Southern Ohio, which are fairly pure mixtures of two or three series of hydrocarbons, those of the series, C_nH_{2n+2} predominating. On account of the present isolation of the latter from carbonaceous matter that could in any manner be associated with their origin, except contiguous beds of coal, their source is not so readily apparent as that of other deposits. While they are for the most part free from sulfur, minute traces of the aromatic hydrocarbons, and oxygen derivatives are generally to be found, and nitrogen derivatives as shown by results to be described in this paper, are apparently everywhere present.

For a more extended discussion of what is here presented, as an introduction to the experimental results of this paper, reference is made to former papers.[1]

That nitrogen bases are generally present in Japan petroleum was shown by Mabery and Takano[2] who found in many samples from different fields, percentages of nitrogen varying from 0.35 to 1.5%. The wide distribution of these bodies in California petroleum appeared in the analysis of 16 samples from as many different fields that gave amounts from 1.0 to 2.55%. Ten samples of Ohio-Trenton Limestone petroleum gave percentages between 0.23 and 0.55%. Engler[3] enumerated the foreign petroleum fields where nitrogen bases have been identified—Germany, Galacia, Rumania, Sumatra, South America, Egypt and Algiers, showing their wide distribution.

These bases have been variously referred to as pyridine and quinoline or their derivatives by those who have separated them, more especially on account of their peculiar odor, and their general properties. In a more extended examination of the basic oil extracted from California petroleum, a series of bases were separated that appeared to be hydroderivatives of methyl quinolines,[4] but further study of their structure two years ago, undertaken in this laboratory at my suggestion by Dr. L. G. Wesson, the results of which are not yet published, appears to indicate that these individual bases are straight methyl quinolines.

With the object in view of demonstrating that the lighter varieties of petroleum in the Eastern fields contain nitrogen bases, through the generous kindness of Mr. Orton C. Dunn[5] of Marietta, O., 5 years ago I was able to procure authentic samples from widely different sections of this territory, and I have since been occupied with the aid of several assistants, a considerable portion of the time in the study of these interesting specimens.

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[1] "Mahone Petroleum, Its Origin and the Origin of Petroleum in General," *J. Ind. Eng. Chem.*, 33, 242 (1914); and "The Relations in Chemical Composition of Petroleum to Its Genesis and Geologic Occurrence," *Econ Geol.*, 1916.

[2] *J. Soc. Chem. Ind.*, 19, 502 (1900).

[3] *Das Erdol*, Leipsic, 1913.

[4] Mabery, *J. Soc. Chem. Ind.*, 18, 504 (1900).

[5] With his scientific education and lifelong connection with the oil and gas industry of this section, there are few men so thoroughly conversant with the geology, manipulation, and technology of the Eastern fields as Mr. Dunn.

The following table presents the descriptive data of these specimens with those of certain heavier varieties:

TABLE I.

Data of Analyzed Specimens.

Serial number	Locality.	Rock strata	Feet in depth	General data.
1	Dudley, O.	Berea grit	1400	Center of Macksburg Field
2	Emblenton, Pa	Rosenberg sand	1240	Jane Oil Co., 2nd sand below Berea grit
3	Malto, Ohio .	First cow run	38	1000 feet from outcrop Well 50 yrs. old. 2 bbls. per day
4	Corning, Ohio .	Berea grit sand	1150	From J. Denman & Son
5	Marietta, O	Goose run sand	150	Uppermost producing strata. East of Mississippi River, 200 feet above Pittsburgh coals
6	Newport, Ohio.	Berea grit	1170	Eureka field
7	Cabin Creek, W. Virginia .	Berea grit	2700	Deepest Berea grit oil sand, running 15 mos.
8	Titusville, Pa.	Third sand	1200	Largest producing sand in Western Pennsylvania
9	Emblenton, Pa.	Third sand	1080	Largest producing sand in Western Pennsylvania
10	Humble Field, Texas, medium	Sand	2750	From Sun Oil Co.
11	Bartlesville, Okla.			
12	Vinton, La. . .		2750	From Texas Oil Co.
13	Mahone Valley.	Pure quartz sand	150	Field flooded by great reservoir
14	Mecca, Ohio	Sand	150	Producing 50 yrs.
15	Sour Lake, Texas	Sand	1300	Sun Oil Co.
16	Beaumont, Texas .	Sand	1000	Sun Oil Co
17	Jennings, La. .	Sand	2000	Texas Oil Co.
18	Caddo, La .	Sand	2200	Sun Oil Co.
19	Humble Field, Texas, light		950–1300	Sun Oil Co.
20	Morris, Kansas			
21	Baku, Russia	Sand		Standard Oil Co.

For the detection of the nitrogen bases and determination of nitrogen 3 methods were employed. As a qualitative test one or two liters of the crude oil was vigorously agitated during several hours with dil. hydrochloric acid, the aqueous solution neutralized with sodium hydroxide and extracted with ether. Every specimen examined left an evaporation of the ether, an oily residue with the characteristic odor of the similar bases extracted from California and Russian petroleum in much larger amounts. The smallest yields were observed from the lightest Berea Grit and Pennsylvania crudes, but even these slight residues redissolved in acid and again precipitated with the alkali. Since acids do not remove completely the basic constituents, quantitative results were not possible by this method.

Volumetric Determination of Nitrogen.

On account of the minute amounts of nitrogen in the crude oils, and the difficulty of burning a large weight of the oil, the details of combustion had to be especially adapted and applied with the utmost care. Since the combustion of a gram of the lighter oils gave only a few tenths of a cc. of nitrogen, the preparation of carbon dioxide of sufficient purity, the removal of nitrogen from the copper oxide and the complete combustion of the gases evolved in analysis altogether formed an extremely laborious task. Next to setting up a vacuum-tight apparatus the most tedious detail was the preparation of carbon dioxide sufficiently free from unabsorbable gas and the removal of this gas from the apparatus. Attempts in the beginning to use magnesite failed on account of the large volume of gas needed, and also because magnesite from several different sources contains a considerable proportion of nitrogenous organic matter that decomposes slowly at the temperature at which carbon dioxide is evolved. Sodium hydrogen carbonate and manganous carbonate are so porous it is impossible to expel by heat all the air from the large amount necessary for the desired volume of carbon dioxide. All commercial potassium carbonate contains at least 0.5% of chloride, and chloride-free it costs $2.00 per lb. But after removal of the chloride by silver sulfate, long operation with this carbonate was unsatisfactory in the removal of nitrogen. As a last resort commercial sodium hydrogen carbonate was found to contain only a trace of chloride that is not objectionable, but on account of its porosity, it persistently retains air. In the preparation of a generator, 12 kg. of this carbonate was partly dissolved in 5 liters of boiling water and the boiling continued for some time, then transferred boiling hot to an 8-liter bottle and the boiling continued by vacuum with frequent shaking, until it was cooled to room temperature and the vacuum finally let down with acid. The generator bottle was closed with a rubber stopper twice perforated for a dropping, glass stoppered, sulfuric acid container, and an exit tube, and the neck inclosed in a wide, sheet iron cup which was filled to nearly the top of the neck with plaster of Paris. Within this enclosure which extended above the stopcock of the acid supply was contained sufficient castor oil to seal the stopper and if necessary the stopcock. The sulfuric acid used for generating carbon dioxide was diluted with an equal volume of water which was kept constant while the mixture was boiled for an hour; it was then partly cooled, quickly poured into a separatory funnel under a layer of gasoline and the funnel kept full of carbon dioxide. As the acid was used in the generator the delivery bulb was also kept full of carbon dioxide. The nitrogen was collected in a Schiff nitrometer with a long capillary extension graduated to tenths of a millimeter. A power pump with a gage graduated to millimeters and capable of exhaustion to less than 0.5 mm. was used for obtaining a vacuum, with a large bottle behind it filled with pumice moistened with sulfuric acid to retain moisture. Between this bottle and a full length manometer was an opening for testing the gas and running it off in large amounts.

Complete combustion of the gases evolved in the analysis of petroleum oils as they are mixed with a large proportion of carbon dioxide requires a high temperature and long contact with copper oxide. While a glass tube must be used for the initial decomposition it cannot withstand the final temperature in vacuum operation. Copper oxide slowly fuses into a quartz tube unless a carborundum sleeve is inserted which is inconvenient, and quartz becomes extremely brittle and breaks easily on continued heating especially at very high temperatures. But it is sufficiently durable for a limited number of determinations, and was used for the combustions that were started in vacuum. For a part of those that were made under atmosphere pressure a steel tube was employed with the advantage that temperatures could be maintained up to the fusion of the copper oxide.

The method of analysis was a combination of the Dumas procedure for nitrogen and the oxygen combustion for carbon. In the glass tube in the rear furnace half filled with copper oxide, a vacant space was reserved for the boat containing the oil with an oxidized copper roll close behind it, in the analysis of the lighter oils, and behind that a large boat filled with fused potassium chlorate. In the forward furnace the quartz or steel tube was filled the length of the furnace with coarse wire copper oxide and the projecting ends were kept cold. Tight joints at the ends of both tubes were maintained with seals of castor oil over rubber stoppers. Other connections were made vacuum tight by means of a special form of thick rubber tube with narrow bore, obtained from the Nela Park laboratory of the General Electric Company, also luted with castor oil.

With all connections of the apparatus properly adjusted the next step was the removal of air which included the film adhering to the entire inner surface, the adsorbed gas from the copper oxide, and most difficult of all that persistently held by the solid hydrogen carbonate. Then with the temperature of the copper oxide in the glass tube held as high as the tube would stand, and in the silica tube at full red heat, the system was repeatedly evacuated and filled with carbon dioxide extending through several days, until tests showed that the unabsorbable gas was removed to the limit of at least one part in 30,000, and combustion of one g. of sugar gave 0.1 cc. of gas not absorbed, when part of the analyses were made, and 0.05 cc. at other times, which were the corrections applied to the specimens of oil analyzed. Continuous operation of the apparatus for two weeks until the supply of bicarbonate in the generator was completely exhausted failed to reduce the amount of unabsorbable gas lower than this limit. Since the nitrogen bases in petroleum are not volatile in air or in vacuum at ordinary temperatures in the analysis of the lighter oils much time was saved by allowing the more volatile hydrocarbons to evaporate in the air to the extent of $^1/_3$ or more of the weight of the oil, and complete combustion of these oils was more readily assured by beginning the analysis under vacuum. Since nitrogen is always held by the residual coke this must be completely burned in a stream of oxygen from the rear potassium chlorate; a slow evolution of oxygen from the

TABLE II.

Percentages of Nitrogen in Specimens of Table I.

Serial number.	Sp gr.	Total wt. of oil.	Cc. of nitrogen	Correction	No. cc in oil.	% nitrogen in oil.	% by Kjeldahl.
1	0 8238	0 6475	0 25	0.09	0.16	0 027	0.022
2	0.8809	0 7890	0.21	0 09	0.1	0.0136	0.014
3	0.8326	0.8707	0 41	0.09	0 32	0.039	0.043
4	0 8404	0 9205	0.45	0.09	0.36	0 41	0.045
5	0.7907	0 9865	0 24	0 09	0 15	0.016	0 019
6	0 7904	1.0876	0.33	0.09	0.24	0.024	0.014
7	0 8139	1 0732	0 39	0 09	0 30	0 029	0.049
8	0 7904	0.7525	0.22	0.09	0.13	0 018	0.01
	..	1.2445	0 15	0.05	0.10	0.01	...
9	0 8007	0.8913	0.19	0.09	0.1	0.012	0 011
	..	1 7550	0.20	0.05	0 15	0.011	...
10	0 9066	0 7535	0.54	0 09	0.45	0.058	0.068
11	0 8625	0.6458	0 58	0 09	0 48	0.074	0.082
12	0 9014	0 6854	0.55	0 09	0.46	0.067	0.079
13	0.9036	0.9023	0.40	0.05	0.35	0.049	0.054
14	0 9023	0.7020	0.35	0.05	0.30	0.054	0.044
15	0.9302	0 8218	0 64	0.09	0 55	0 067	0 082
16	0 9175	0.5630	0.25	0 09	0.16	0 023	0 016
17	0.9054	0.6220	0.39	0.09	0.30	0.48	0 039
18	0 8584	0.6000	0 39	0 09	0 30	0.050	0.057
19	0.8227	1.9985	0.39	0.09	0.30	0.015	0.017
20	0.8499	0.9870	0.44	0.09	0.35	0.035	0.045
21	0 8650	0.7021	0.45	0 05	0.40	0.071	0.06
Coke (No. 7) from 1000 g. oil, 70 g. coke		1.6501	1.8	0.09	1.76	0.13	...
Nitrogen from oil retained in coke						0.009	...

beginning of the combustion without the aid of the copper roll is sufficient to prevent backward distillation, and it aids the forward movement and partial burning of the gases. After the oil is completely burned the tubes are swept clear of nitrogen with carbon dioxide from the generator, and the reduced copper oxide reoxidized with tank oxygen. If this be done with the tubes hot, after a few evacuations the system is ready for the next analysis. Even with this large surface of copper oxide the combustion cannot be pushed too rapidly for unburned gases will escape. One g. of oil requires two to three hours in safe operation. The average room temperature, 25°, and the average barometer readings 740 mm. were used in the reduction of the volume of nitrogen to standard conditions. In the preceding table are presented the data of the volumetric determinations together with analysis of the same specimens by the Kjeldahl method using 5 g. of the oil, which were made by Professor M. F. Coolbaugh.

Summary.

Proof has been given of the presence of nitrogen in petroleum of all the principal oil fields, in forms of combination that could have had their origin only in the remains of vegetable or animal bodies. Presumptive evidence has been shown that the associated hydrocarbons in petroleum had the same origin.

A special method of analysis for the determination of minute proportions of nitrogen in oils is described.

CLEVELAND, OHIO

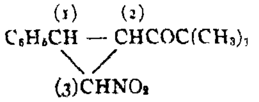
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY.]

STUDIES IN THE CYCLOPROPANE SERIES. IX. NITROCYCLOPROPANE DERIVATIVES.

BY ELMER PETER KOHLER AND M. SRINIVASA RAO

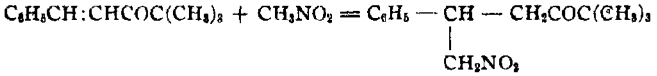
Received August 27, 1919

The following paper deals with a cyclopropane derivative which has an alkyl group in place of one of the aryl groups contained in all the nitrocyclopropane derivatives described in earlier papers. Substances of this type are not easily made. In order to avoid complications in preparation it finally proved necessary to use tertiary butyl compounds. The substance studied, therefore, was phenyl-trimethylacetyl-nitrocyclopropane:

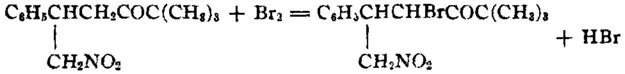


$$\overset{(1)}{C_6H_5CH} - \overset{(2)}{CHCOC(CH_3)_3} \atop {\diagdown\ \diagup \atop (3)CHNO_2}$$

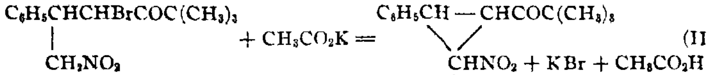
This substance was made without much difficulty by adding nitromethane to benzalpinacoline, brominating the addition product, and eliminating hydrogen bromide from the resulting bromo compound:



$$C_6H_5CH{:}CHCOC(CH_3)_3 + CH_3NO_2 = C_6H_5-\underset{\displaystyle CH_2NO_2}{\underset{|}{CH}}-CH_2COC(CH_3)_3 \qquad (I)$$



$$\underset{\displaystyle CH_2NO_2}{\underset{|}{C_6H_5CH}}CH_2COC(CH_3)_3 + Br_2 = \underset{\displaystyle CH_2NO_2}{\underset{|}{C_6H_5CH}}CHBrCOC(CH_3)_3 + HBr \qquad (II)$$



$$\underset{\displaystyle CH_2NO_2}{\underset{|}{C_6H_5CH}}CHBrCOC(CH_3)_3 + CH_3CO_2K = C_6H_5\underset{\displaystyle CHNO_2}{\underset{\diagdown\;\diagup}{CH-CH}}COC(CH_3)_3 + KBr + CH_3CO_2H \qquad (III)$$

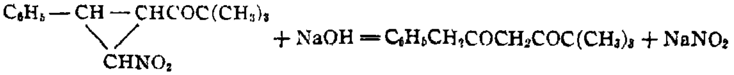
The reactions are similar to those used in the earlier work but the bromo compound does not give up hydrogen bromide nearly so easily as the corresponding substances containing only aryl groups, hence the yield of cyclopropane derivative was smaller.

The substitution of a tertiary butyl for a phenyl group, as was to be expected, does not materially alter the chemical properties of the cyclopropane derivative. Unfortunately it also does not lower the boiling point of the products obtained from the cyclopropane derivative sufficiently to make separations by vacuum distillation feasible—one of the advantages we hoped to gain by the substitution.

The cyclopropane derivative readily combines with other substances; the ring in all cases opens between carbon atoms (1) and (2). The structure of the products was established with less difficulty than we anticipated. Thus with bases the substance gave a product which has the composition $C_9H_{18}O_2$, and which must be a diketone because it gives a copper derivative when shaken with a solution of copper acetate, and two isomeric isoxazole derivatives when treated with hydroxylamine. The structure of this di-ketone was established by synthesis from ethyl phenylacetate and pinacoline:

$$C_6H_5CH_2COOC_2H_5 + CH_3COC(CH_3)_3 = C_6H_5CH_2COCH_2COC(CH_3)_3 + C_2H_5OH.$$

It is evident that this substance can be formed from the cyclopropane derivative only by opening the ring between carbon atoms (1) and (2), the reaction being expressed by the equation.

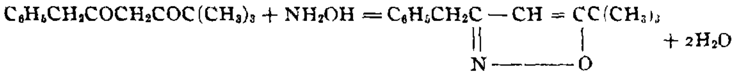


$$C_6H_5-\underset{\displaystyle CHNO_2}{\underset{\diagdown\;\diagup}{CH-CH}}COC(CH_3)_3 + NaOH = C_6H_5CH_2COCH_2COC(CH_3)_3 + NaNO_2$$

The product obtained by adding hydrogen bromide to the cyclopropane derivative has the composition $C_{14}H_{18}O_3NBr$. It very easily loses both nitrous and hydrobromic acids, but by cautious treatment with potassium acetate it is possible to convert it into an unsaturated nitro compound which is isomeric with the cyclopropane derivative, $C_{14}H_{17}O_3N$, and which must have a double linkage next to the phenyl group because it gives benzaldehyde as one of the oxidation products. When this unsaturated nitro compound is treated with hydrogen bromide in glacial acetic acid it not only adds hydrobromic acid but also undergoes reduction, the reaction being expressed by the equation:

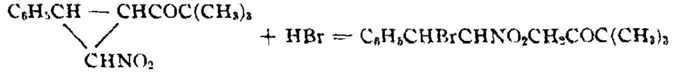
$$C_{14}H_{17}O_3N + 3HBr = C_{14}H_{16}ONBr + Br_2 + 2H_2O.$$

The resulting bromine compound, finally, when reduced with zinc gives one of the isoxazole derivatives that is obtained from the β-diketone in accordance with the equation:



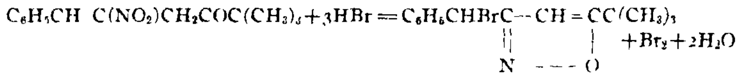
$$C_6H_5CH_2COCH_2COC(CH_3)_3 + NH_2OH = \begin{array}{l} C_6H_5CH_2C - CH = CC(CH_3)_3 \\ \qquad\qquad \| \qquad\quad | \\ \qquad\qquad N \text{———} O \end{array} + 2H_2O$$

This relation establishes the structure of all the intermediate products, the successive reactions being represented by the following equations:

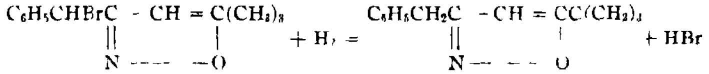


$$\begin{array}{l} C_6H_5CH - CHCOC(CH_3)_3 \\ \quad \diagdown \diagup \\ \quad CHNO_2 \end{array} + HBr = C_6H_5CHBrCHNO_2CH_2COC(CH_3)_3 \qquad (I)$$

$$C_6H_5CHBrCHNO_2CH_2COC(CH_3)_3 - HBr = C_6H_5CH.C(NO_2)CH_2COC(CH_3)_3 \qquad (II)$$



$$C_6H_5CH\ C(NO_2)CH_2COC(CH_3)_3 + 3HBr = \begin{array}{l} C_6H_5CHBrC - CH = CC(CH_3)_3 \\ \qquad\qquad \| \qquad\quad | \\ \qquad\qquad N \text{———} O \end{array} + Br_2 + 2H_2O \qquad (III)$$



$$\begin{array}{l} C_6H_5CHBrC - CH = C(CH_3)_3 \\ \qquad\quad \| \qquad\quad | \\ \qquad\quad N \text{———} O \end{array} + H_2 = \begin{array}{l} C_6H_5CH_2C - CH = CC(CH_3)_3 \\ \qquad\quad \| \qquad\quad | \\ \qquad\quad N \text{———} O \end{array} + HBr \qquad (IV)$$

Experimental Part.

γ-Nitro-β-phenyl-propyl-tertiary butyl ketone, $NO_2CH_2CH(C_6H_5)CH_2COC(CH_3)_3$.—A very concentrated solution of sodium methylate containing 3 g. of sodium was added to a solution of 19 g. of benzalpinacoline and 4 g. of nitromethane in 45 cc. of dry methyl alcohol. The mixture was shaken until all of the sodium nitromethane had gone into solution and then immediately cooled in ice water. The well cooled yellow or orange colored solution was acidified with glacial acetic acid which was added drop by drop while the mixture was stirred vigorously. This precipitated the product as a white powder contaminated with a small quantity of oil and with sodium compounds that are held tenaciously. The powder was washed with cold methyl alcohol to remove the oil and then very thoroughly with water to remove sodium compounds. This left a colorless product which after drying was sufficiently pure for bromination. For the purpose of analysis it was crystallized from methyl alcohol from which it separated in minute colorless plates.

Calc. for $C_{14}H_{19}O_3$ C, 67.4, H, 7.7. Found C, 67.1; H, 7.5.

The nitro-ketone is readily soluble in all common organic solvents except ligroin. It melts at 74°. The yield was 80 to 90%.

γ-Nitro-β-phenyl-α-bromo-propyl-tertiary butyl ketone, $NO_2CH_2CH(C_6H_5)CHBrCOC(CH_3)_3$.—For the purpose of bromination the nitroketone was, as usual, suspended in a small quantity of chloroform or carbon tetrachloride. With the pure substance the reaction starts promptly at the ordinary temperature, but the crude washed and dried product usually has to be heated to the boiling point of the solvent. The ketone dissolves as the reaction proceeds and the bromo compounds generally begin to separate before it is complete. After adding a slight excess of bromine the solvent was removed under diminished pressure and the solid residue washed repeatedly with small quantities of methyl alcohol. This left a colorless mass composed mainly of two isomeric α-bromo compounds. The yield of mixed bromo compounds was 92%.

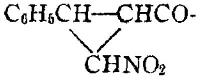
In order to separate the mixture of monobromo compounds it was first extracted two or three times with small quantities of boiling methyl alcohol. The residue—composed mainly of the higher melting substance—after several crystallizations from methyl alcohol gave a product which separated in large needles melting constantly at 143–144°. This bromo compound is sparingly soluble in methyl and ethyl alcohols, moderately in chloroform and carbon tetrachloride, readily in acetone.

Calc for $C_{14}H_{18}O_3NBr$ C, 51.2, H, 5.5 Found C, 50.9, H, 5.6

The lower melting compound was obtained by repeated recrystallization of the solid that separated from the first methyl alcoholic extract of the mixed substances. It separated in colorless plates which melted at 74–75°.

Calc for $C_{14}H_{18}O_3NBr$ C, 51.2, H, 5.5 Found C, 51.3, H, 5.8

1-Phenyl-2-trimethylacetyl-3-nitro cyclopropane,



$C_6H_5CH{-}CHCO{-}C(CH_3)_3$ (ring closed through $CHNO_2$)

$C(CH_3)_3$.—The lower melting bromo compound is stable in boiling methyl alcohol but it is rapidly converted into the higher melting isomer by methyl alcoholic potassium acetate. Thus a pure specimen melting at 75° was boiled with methyl alcohol for nearly an hour without change in melting point but when boiled for another hour after a little potassium acetate had been added to the solution it melted sharply at 145°. Both bromo compounds, consequently, give the same cyclopropane derivative. This was, therefore, commonly made by starting with the mixed bromo compounds.

The elimination of hydrobromic acid is so difficult that it is not feasible to transform a given quantity of the bromo compounds completely into cyclopropane derivative in a single operation, for after the concentration of the cyclopropane derivative reaches a certain point, boiling potassium acetate decomposes it as rapidly as it removes hydrogen bromide from the bromo compounds. The most satisfactory procedure was as follows.

A concentrated solution of 25 g. of the mixed bromo compounds in methyl alcohol is boiled with 8 g. of potassium acetate for half an hour.

Eight g. more of potassium acetate is then added gradually to the boiling solution, and the mixture refluxed for another 15 minutes. Half of the methyl alcohol is now distilled off and the residue cooled in a freezing mixture. The resulting solid is washed first with a little methyl alcohol, then with water until free from bromide. The colorless solid remaining is dissolved in the minimum amount of boiling methyl alcohol and the solution allowed to cool. It deposits the cyclopropane derivative in large transparent cubes which after washing with methyl alcohol are analytically pure. The filtrate may deposit some more cubical crystals but the second crop generally is a mixture composed largely of needles of the higher melting bromo compound. While the mixture may be separated mechanically, it is more economical to repeat the treatment with potassium acetate.

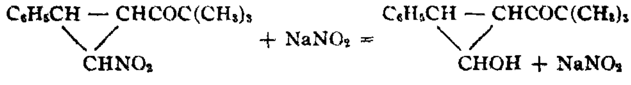
The yield of pure cyclopropane derivative was about 60%—the substance crystallizes in cubes and melts at 94°. It is readily soluble in all common organic solvents except ligroin.

Calc for $C_{14}H_{17}O_3N$ C, 67.9, H, 6.9 Found C, 67.5, H, 6.7

Action of Alkalies.—The cyclopropane derivative is readily attacked by alkalies. These invariably remove nitrous acid from the substance and under most conditions they transform it into a number of oily products from which it is impossible to isolate pure compounds. The following procedure, however, gave a fair yield of a solid product: A concentrated solution of sodium methylate containing 6 g. of sodium in 50 cc. of dry methyl alcohol was added slowly and with constant shaking to a suspension of 20 g. of the cyclopropane derivative in 15 cc. of the same solvent, which was cooled in ice water. The mixture was then vigorously shaken on a machine. After several hours, during which all of the substance dissolved and most of the sodium nitrite separated, it was transferred to a vacuum desiccator and evaporated to complete dryness over sulfuric acid. This left an orange colored residue composed mainly of sodium nitrite and an organic sodium compound. The latter was extracted with methyl alcohol and the well cooled solution cautiously acidified with sulfuric acid. The resulting solid was purified by recrystallization from methyl alcohol.

Calc for $C_{14}H_{18}O_2$ C, 77.1, H, 8.2 Found C, 77.2, H, 8.4

The composition of the substance indicated replacement of the nitro group by hydroxyl:



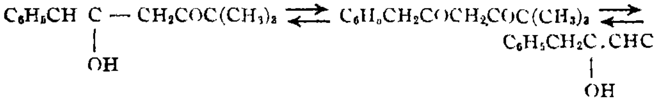
$$\begin{array}{c}C_6H_5CH - CHCOC(CH_3)_3\\ \diagdown\ \diagup\\ CHNO_2\end{array} + NaNO_2 = \begin{array}{c}C_6H_5CH - CHCOC(CH_3)_3\\ \diagdown\ \diagup\\ CHOH\end{array} + NaNO_3$$

The properties of the substance, however, could not be reconciled with such a formula; for while it formed a phenylcarbamate with phenylisocyanate, it gave a color reaction with ferric chloride, formed a sodium derivative with sodium ethylate and a copper derivative with copper acetate, and was converted into an isoxazole by hydroxylamine. These are characteristic reactions of β-diketones.

The two β-diketones that might be formed from the cyclopropane derivative are represented by the formulas. $C_6H_5CH_2COCH_2COC(CH_3)_3$, $C_6H_5COCH_2COCH_2C(CH_3)_3$. Inasmuch as the substance gives phenylacetic acid and pinacoline when boiled with alcoholic potassium hydroxide it can not have a benzoyl group. This excludes the second formula. We therefore undertook the synthesis of phenylacetyl-trimethylacetylmethane. For this purpose 2 3 g of sodium was added to a well cooled solution of 32 g. of ethyl phenyl acetate and 15 g. pinacoline in 150 cc. of dry ether. The solution was kept in ice water for several hours, then at the ordinary temperature until all of the sodium had disappeared. It was then acidified, extracted with sodium hydrogen carbonate until free from phenylacetic acid, and finally shaken with a cold saturated solution of copper acetate. This precipitated a pale green copper derivative which when shaken with hydrochloric acid and a little ether gave the same substance that had been obtained from the cyclopropane derivative:

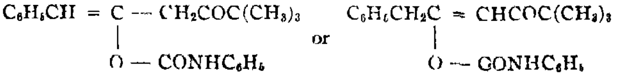
$$C_6H_5CH_2CO.OC_2H_5 + CH_3COC(CH_3)_3 = C_6H_5CH_2COCH_2COC(CH_3)_3 + C_6H_5OH$$

Phenacetyl-trimethyl acetyl-methane is readily soluble in ether, moderately in alcohol, very sparingly in ligroin. It crystallizes in needles and melts at 44°. In alcoholic solution it gives a deep red color with ferric chloride. When it is oxidized with permanganate in acetone it gives almost exclusively benzoic and trimethyl acetic acids while when oxidized in alkaline solution with aqueous permanganate the sole organic products are phenylacetic and trimethylacetic acids. It is, therefore, evidently capable of enolizing in two different ways:



$$\underset{\displaystyle OH}{C_6H_5CH\ \overset{}{C}} - CH_2COC(CH_3)_2 \rightleftarrows C_6H_5CH_2COCH_2COC(CH_3)_3 \rightleftarrows \underset{\displaystyle OH}{C_6H_5CH_2C}.CHCOC(CH_3)_3$$

The phenylcarbamate of the diketone:

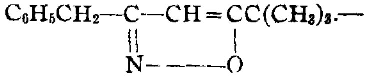


$$C_6H_5CH = \underset{\displaystyle O - CONHC_6H_5}{C} - CH_2COC(CH_3)_3 \quad \text{or} \quad C_6H_5CH_2\underset{\displaystyle O - CONHC_6H_5}{C} = CHCOC(CH_3)_3$$

To prepare the carbamate, a mixture of 5 g. of the diketone and 5 g. of phenylisocyanate was heated to 100° for 15 minutes and then to 140–150° for 10 minutes more. The resulting pasty solid was washed with benzene and ether, and recrystallized from methyl alcohol. It is readily soluble in chloroform and acetone, moderately in boiling methyl alcohol, very sparingly in ether. Its melting point is 130–132°.

Calc. for $C_{21}H_{23}O_3N$: C, 74.8, H, 6.8 Found C, 74.9, H, 6.8.

5-Benzyl-3-tertiarybutyl Isoxazole, $C_6H_5CH_2$—C—CH = CC$(CH_3)_3$.—

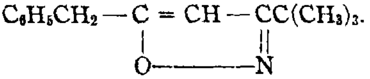


$$\begin{array}{l} C_6H_5CH_2\text{—}C\text{—}CH=CC(CH_3)_3 \\ \qquad\qquad\quad\ \| \qquad\quad\ | \\ \qquad\qquad\quad N\text{———}O \end{array}$$

A solution of 3 g. of the diketone, 3 g. of hydroxylamine hydrochloride and 5 g. of potassium hydroxide in 100 cc. of methyl alcohol was refluxed for half an hour and then poured into ice water. This precipitated a granular, white solid which after recrystallization from dilute methyl alcohol melted as 51°.

Calc. for $C_{14}H_{17}ON$: C, 78.1; H, 7.9; N, 6.5. Found: C, 78.1, H, 7.8; N, 6.9.

3-Benzyl-5-tertiarybutyl Isoxazole, $C_6H_5CH_2$ — C = CH — CC$(CH_3)_3$.



$$\begin{array}{l} C_6H_5CH_2\text{—}C=CH\text{—}CC(CH_3)_3 \\ \qquad\qquad\quad\ | \qquad\qquad\ \| \\ \qquad\qquad\quad O\text{————}N \end{array}$$

—The alkaline filtrate from the isoxazole, on acidification gave another product which after recrystallization from dilute methyl alcohol melted at 63°. The analyses show that this is an isomeric isoxazole.

Calc for $C_{14}H_{17}OH$ C, 78.1, H, 7.9 Found C, 78.1; H, 8.0

β-Nitro-γ-bromo-γ-phenyl-propyl tertiarybutyl Ketone, C_6H_5CHBr-$CHNO_2CH_2NO_2COC(CH_3)_3$.—The nitro cyclopropane combines very readily with hydrobromic acid both when dissolved in alcohol and in glacial acetic acid. A solution in glacial acetic acid cooled in ice water was saturated with hydrogen bromide, allowed to stand for a few minutes, and poured into ice water. This precipitated a colorless oil which solidified when rubbed with a glass rod. The product after washing with ice water until free from acid, and drying *in vacuo* melted at 66–67° and the melting point remained the same after recrystallization from methyl alcohol or from ether and ligroin. The yield was quantitative.

Calc for $C_{14}H_{18}O_3NBr$: C, 51.4; H, 5.5. Found: C, 51.7, H, 5.5.

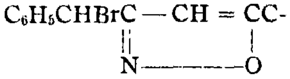
The bromo compound is exceedingly unstable. It loses both nitrous and hydrobromic acids and passes into oily products when boiled with methyl alcohol, and even cold solutions rapidly become acid. When the pure, dry substance is kept in a stoppered bottle it loses nitrous acid, and gradually turns into a brown oil. Potassium acetate, in the cold, eliminates principally hydrobromic acid and forms an unstable nitro compound.

β-Benzal-β-nitro-ethyl tertiarybutyl Ketone, $C_6H_5CH:C(NO_2)CH_2$-$COC(CH_3)_3$.—To an ice cold solution of 9 g. of the hydrobromic acid addition product in 30 cc. of methyl alcohol, 4 g. of powdered potassium acetate was added in small portions and with constant shaking. The solution first turned yellow, then brown, while potassium bromide and a little potassium nitrate was deposited. After standing for 12 hours in an ice chest, most of the organic product had separated as a yellow solid.

This was thoroughly washed with water and recrystallized from methyl alcohol.

Calc. for $C_{14}H_{19}O_3N$: C, 67.9; H, 6.6 Found. C, 67.9; H, 6.9.

The unsaturated nitro compound crystalizes in long, yellow needles and melts at 53–54°. It is readily soluble in the common organic solvents. Its solution in acetone instantly reduces permanganate, and benzaldehyde is a primary oxidation product, showing that the double linkage is next to the phenyl group.

5-Bromobenzyl-3-tertiarybutyl Isoxazole,  $$\begin{array}{l} C_6H_5CHBrC{-}CH{=}CC{-}(CH_3)_3 \\ \qquad\qquad\;\; \| \qquad\quad\;\; | \\ \qquad\qquad\; N{-}{-}{-}{-}O \end{array}$$ $(CH_3)_3$.—When hydrogen bromide was passed into a solution of the unsaturated nitro compound, the color of the solution rapidly changed from yellow to red owing to separation of free bromine. The solution was saturated at 0°, allowed to stand for several hours in an ice chest and then poured into ice water. This precipitated an oil which solidified when rubbed. The solid was washed with sodium hydrogen sulfite until colorless, and purified by recrystallization from methyl alcohol.

Calc for $C_{14}H_{16}ONBr$; C, 57.1; H, 5.4 Found C, 56.8, H, 5.6

The isoxazole derivative crystallizes in needles and melts at 77–78°. It is quite stable, being recovered unchanged after having been heated to 150° for 8 hours. The bromine is readily replaced with hydrogen. Thus 0.5 g. of the substance and one g. of zinc dust were heated in acetic acid on a steam bath for half an hour. The solution was filtered into ice water, and the precipitated solid recrystallized from methyl alcohol. It was bromine free, melted at 50°, and the melting point remained the same when it was mixed with a specimen of the lower melting isoxazole which had been obtained by the action of hydroxylamine upon the diketone.

CAMBRIDGE, MASS

NOTE.

Correction.—In the review of "Chemistry in Old Philadelphia,"[1] line 20, read: Hare's oxy-hydrogen blow pipe and some of Woodhouse's and some of Hare's other contributions. F. B. DAINS.

NEW BOOKS.

Intermediate Text-Book of Chemistry. 1st edition. By ALEXANDER SMITH, Head of Department of Chemistry, Columbia University. The Century Co., New York, 1919. vi + 520 pp. 115 figs. 14 × 21 cm. $2.25.

This is a new member of the successful series of Smith texts, now four in number. Together they carry out the best traditions of chemical instruction in this country, as did the Remsen series of the preceding generation, and are as nearly standard as any author may expect to reach. The "Intermediate Text-Book" seems adapted to the diversified students in colleges and in technical and normal schools who do not require an elaborate chemical training. After an inviting and masterly introduction dealing with chemical processes in every-day life the author takes up the subject matter in the usually accepted order, enriching the treatment with the essentials of physical chemistry, clearly presented and properly emphasized. Chemical arithmetic could hardly be better handled than here. Review questions follow each chapter.

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[1] THIS JOURNAL, 41, 1315 (1919).

There are slight departures from judicious text-book writing in the controversial paragraph on the history of oxygen (p. 28) and in selecting Lomonossov and Mayow for two of the three full-page portraits. The author is inclined to amplify the list of definitions (*e. g.*, constituent, dilute solution, concentrated solution). His statement that' "There are no laws in nature" (p. 23) will meet with wide disapproval, for there are several rules of behavior in nature which to all but skeptical philosophers are so certain and constant as to be equivalent to decrees imposed by a controlling authority. Something seems to be omitted in approaching the concept of ions (p. 168); the introduction of the term is abrupt. The electron theory is handled very conservatively and the recent general acknowledgment of the reality of molecules has not led the author to modify his treatment of the atomic and molecular theories. The descriptive chemistry is brought up to the end of 1918; we read that "helium is now being used to fill balloons." The type is clear; textual errors are few; the index is a compromise in length between English and American customs.

HERMON C. COOPER.

Introduction to Organic Chemistry. 2nd edition. By JOHN TAPPAN STODDARD, Professor of Chemistry in Smith College. P Blakiston's Son and Co., Philadelphia, 1918. xi + 423 pp. 13 × 18 cm. $1.50 net.

The preface to the second edition of the text states that "The favorable reception accorded the text has encouraged me to take advantage of this year's reprinting to make a number of corrections and changes that have been suggested during the four years since it appeared."

The changes made are not extensive but add to the value of the text. They consist in minor additions to such subjects as "General Methods for the Formation of Paraffins," "Grignard's Synthesis" and "Artificial Rubber." Some new compounds are introduced such as antipyrene and salvarsan. Additions of from one to two pages have been made in the discussion of each of the following subjects: Natural Fats and Oils, Uric Acid and the Purine Bases, and Proteins. There is also added a two-page table on "Ionization Constants of Some Organic Acids and Bases."

It is unfortunate that the publisher did not renumber the pages. Such figures as 160*a*, 160*b*, do not leave a good impression on the mind, suggesting additions of the patch work variety which is not warranted in the case of the text.

The author has succeeded in bringing into relatively small compass as extended a discussion of the subject of organic chemistry as can be thoroughly digested by students in the time ordinarily allotted to the introductory course in this subject. Of course, there is always a danger that in the attempt to concentrate one may overdo the thing and devitalize the subject. It is never fair, however, to expect too much of a text-book; the teacher must be taken into account.

There is certainly much to be said in favor of limiting the ground covered in the introductory course as Professor Stoddard has done. Pope might have been writing of the domain of organic chemistry when he penned the line,

"A mighty maze but not without a plan."

If we are not on our guard our students will comprehend that it is a "mighty maze" indeed, but fail to get "the plan." WM. MCPHERSON.

VOL. XLI. NOVEMBER, 1919. NO. 11.

THE JOURNAL

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American Chemical Society

with which has been incorporated the

American Chemical Journal
(Founded by Ira Remsen)

[CONTRIBUTION FROM THE LABORATORY OF PHYSICAL CHEMISTRY OF THE UNIVERSITY OF ILLINOIS. PUBLICATION NO. 35.]

SOME PHYSICAL PROPERTIES OF MANNITE AND ITS AQUEOUS SOLUTIONS.[1]

BY JOSEPH M. BRAHAM.

Received June 21, 1919.

This study was made in connection with an investigation on the laws of aqueous solutions. The compound, which is also termed mannitol and hexanhexol, is of interest in the latter connection since it contains a comparatively large number of hydroxyl groups. The literature on the subject is not very complete and very little recent work has been done on it. This paper presents the results of the study and includes a brief statement of earlier work on the subject.

I. Purification of Mannite.

An investigation was first made to ascertain the number of recrystallizations of commercial mannite that are required to yield a pure product, the melting point being the criterion of purity. The material was dissolved in distilled water at a temperature near 80°, forming an almost saturated solution. This solution was filtered to remove the suspended impurities which were present in considerable quantity, then cooled to about 40° and alcohol added to reduce the solubility. The crystals were freed from the liquid as completely as possible and then dried in an electric oven at 120–130° for several hours The second crystallization was made by dissolving the crystals, from which the mother liquor had been removed, in pure, hot water, allowing the solution to cool and then adding alcohol; a similar procedure was followed in the third and fourth crystallizations. Another lot was purified in precisely the same manner except that no alcohol was used and contact of the crystals with the filter paper was avoided, but no difference in the purity of the two lots could be distinguished.

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[1] This article is based on a thesis submitted by the writer in 1915 to the Graduate School of the University of Illinois in partial fulfillment of the requirements for the degree of Master of Science.

II. Melting Point of Pure Mannite.

The most extensive set of determinations described in the literature was made by Landolt.[1] He found the freezing point of a mass consisting of 620 g. of mannite to be 165 69°, with a much smaller quantity of material the melting point was 165 73° and the freezing point 165 64°. Using an apparatus designed to avoid stem correction, the values 166.97° and 167 04° were obtained; the latter values are undoubtedly too high. The results obtained by other investigators are. Favre,[2] 166° (freezing point 162°), Stohmann and Langhein,[3] 166°; and Kroft and Dyes,[4] 166°. Since the true value is thus uncertain, this property was investigated.

A nitrogen filled mercury thermometer which had been checked by the Bureau of Standards was employed. It was graduated in 0 1°, ruled directly on the stem, readings to 0 01° were made with the aid of a reading glass. Three auxiliary thermometers were employed to determine the temperature of the emergent stem at various heights. The equilibrium mixture of mannite crystals and liquid was contained in a small Dewar tube closed by a tin foiled cork and stirred with a small glass rod with a loop at one end. The mannite was heated to about 175°.in an electric oven or very carefully over a gas flame and the liquid poured into the previously heated Dewar tube. It was found impossible to obtain a perfectly clear liquid by either method of heating, the slight brown color seeming to indicate that carbonization occurs to a very limited extent, the color was first ascribed to the presence of fine filter paper shreds, but it was later observed in fused material with which special precautions had been taken to avoid contamination from that source. When the temperature of the liquid in the Dewar had dropped to about 170°, pure crystals were added. A temperature which remained constant for several minutes was soon reached. The following results were obtained:

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[1] *Z physik Chem*, **4**, 366 (1889)

[2] *Ann. chim phys*, [3] **11**, 71 (1844).

[3] *J. prakt Chem*, [2] **45**, 305 (1892)

[4] *Ber*, **28**, 2583 (1895)

Mannite.	Melting point.
Original material.	165 10°
First crystallization	165 84
Second crystallization	166 05
Third crystallization	166 05
Fourth crystallization	166 05

It is evident from these data that two crystallizations of commercial mannite are necessary as well as sufficient for the production of pure mannite.

III. Specific Rotation.

Of the 3 optical forms of mannite, the so-called dextro form, which is actually levorotatory, is the most common. Very few determinations of the specific rotation of pure mannite in aqueous solutions have been made, although the literature contains numerous references to measurements on solutions of mannite with some other constituent such as borax, boric acid or sodium hydroxide. In 1873, G. Bouchardat[1] found that the rotation was less than 0.2° which was the smallest value then measurable, but the fact that it really was optically active was shown the following year by L. Vignon[2] in his researches on mannite solutions containing borax or boric acid. Using a greatly improved apparatus, G. Bouchardat[3] later found the specific rotation to be $[\alpha]_j = -0.25°$ (estimated to be $-0.23°$ referred to the sodium D line), the temperature of the solution not being given. In 1875, L. Vignon[4] again studied this property of mannite in pure aqueous solutions and found the following values, each of which is the average of 10 readings: $[\alpha]_D = 0.204°$, $0.260°$, and $0.232°$. The temperature of the solution was not stated.

Since no more recent determinations had been made, it seemed desirable to determine this constant with greater accuracy. A sample of purified mannite was fused to eliminate completely all traces of moisture and then finely powdered; but solutions from this material possessed a slight brown color which made satisfactory illumination of the solution impossible. Samples which had been thoroughly dried but not fused were therefore used. The solutions were prepared by dissolving 17.6067 g. of mannite in distilled water and making up to 100 cc. at 25°.

A triple field Schmidt and Haensch polarimeter fitted with a 100 cm. jacketed tube was used, and the solution under examination kept at 25°. A quartz mercury vapor lamp furnished the light, which was further purified by passing it through a spectroscope, the green E-line of mercury being employed. The specific rotation was found to be $[\alpha]^{25}_E = -0.244° \pm 0.002$. The values of $-0.244°$ and -0.245 ± 0.002 were obtained at the same time by Mr. C. Scholl in this laboratory. Assuming that the same factor (0.8509)[1] may be used in converting the value referred to the mercury E line to the sodium D line as found for quartz, the rotation becomes $[\alpha]_D^{25} = -0.208 \pm 0.002$.

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[1] *Compt. rend.*, **76**, 1550 (1873)

[2] *Ibid.*, **77**, 1191 (1874).

[3] *Ibid.*, **80**, 122 (1875).

[4] *Ann. chim. phys.*, [5] **2**, 440 (1875).

IV. Solubility-Freezing-Point Measurements.

At the time this investigation was begun, the data on the solubility of mannite in water and on the freezing points of relatively concentrated solutions were very meager. The solubility data contained in the literature are summarized in the following table:

Solvent	Temp Degrees	G mannite per 100 g of solvent	Investigator
Water	14	12.8	H. D Krusemann[2]
Water	16	16.0	Wanklyn-Erlenmeyer[3]
Water	18	15.6	M Berthelot[4]
Water	23	18.5	M Berthelot
Water	24.5	20.96	A Findlay[5]
Water	35.8	29.03	A Findlay
Water	50.8	46.69	A Findlay
Ethyl alcohol (d = 0.8085	15.0	1.2	M Berthelot[4]
Ethyl alcohol (absolute	14	0.07	M Berthelot

It was planned to obtain the complete freezing-point solubility diagram for the system mannite water but difficulties, later referred to, limited the study to the temperature range between the eutectic point and 103°.

1. **Apparatus.**—The freezing point-solubility apparatus employed for measurements near and below zero is shown in Fig. 1. The metal container was completely surrounded by a mixture of water and cracked ice. For solubility determinations at higher temperatures, the Dewar vessel was surrounded by an electrically heated oil bath maintained at the proper temperature. A mechanical stirrer was used in the solutions. A standardized Beckmann thermometer was used near and below zero, a standard Baudin thermometer for temperatures near 25°, and a standardized thermometer graduated between 50° and 110° in 0.05° division for temperatures of 50° and higher. The Beckmann was checked against a standard Baudin thermometer over the range employed, readings being made to 0.001° with the aid of a telescope equipped with a vernier.

2. **Method of Sampling.**—The method of removing samples from the system for analysis and the types of filter are shown in Fig. 1. A filter consisting of a short alundum tip sealed into a hard glass tube proved

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[1] Bur. Standards, *Bull* **2,** No 2

[2] *Ber.*, **9,** 1467 (1876).

[3] *J. prakt. Chem* , **88,** 297 (1863)

[4] *Ann. chim phys* , [3] **47,** 301 (1856)

[5] *J. Chem Soc.*, **81,** 1219 (1902)

to be very satisfactory for solutions up to 50. With solutions of greater viscosity, however, it was necessary to use a filter of less resistance since the suction necessary to draw the solution through the alundum tip caused vaporization to occur within the sampling tube, and a cotton plug placed in the constricted end of a glass tube was therefore used to filter these solutions. It was evident that crystals did not pass through the cotton since the solution rising in the withdrawal tube did not quickly crystallize when exposed to the lower temperature in the upper part of the tube, as would have been the case if crystals had been present. At the higher temperatures the solution became so viscous that its passage even through the cotton was extremely slow, requiring a careful adjustment of the suction to avoid evaporation as the liquid emerged from the cotton. To prevent crystallization in the tube during this rather slow

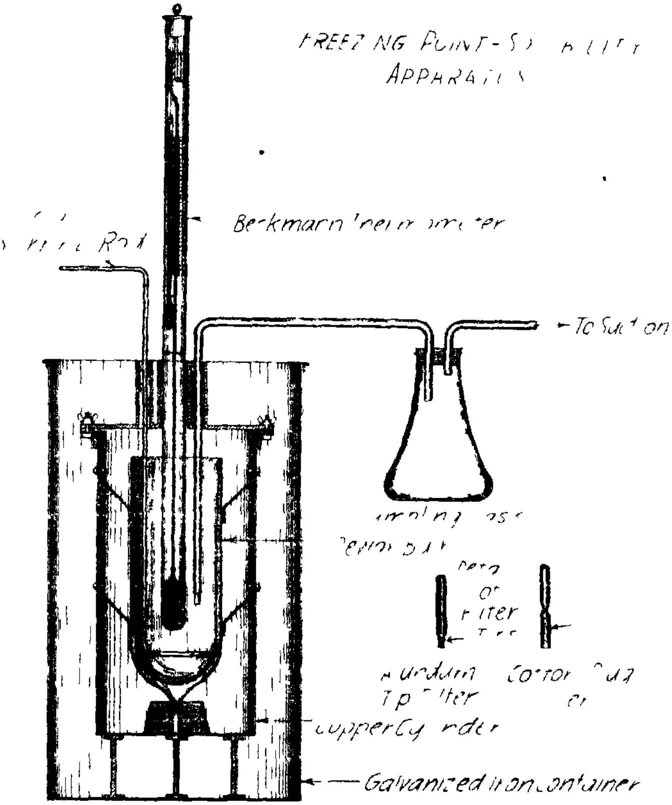

FIG 1

Scale 1:6

process the upper part of the withdrawal tube was therefore heated electrically, but even with this precaution, solidification occurred in several instances. The first portion of the solution withdrawn was discarded, the sample taken for analyses being collected in a weighed flask.

3. **Analysis of Solutions.**—The quantity of mannite in a given sample was determined by an interferometer, the use of which has been described in detail by L. H. Adams.[1] The instrument was calibrated by determining the readings at 25° on mannite solutions of known composition as follows:

G. mannite (weights *in vacuo*) per 1000 g. of water *C*	Reading of interferometer at 25° *r*	*C/r*
11.806	7.77	1.5194
15.881	10.46	1.5183
23.336	15.48	1.5075
26.090	17.37	1.5020
26.594	17.72	1.5008
31.001	20.84	1.4876
37.808	25.79	1.4660

A curve was constructed from these data in which the ratio *C/r* was plotted against *r*. It was necessary to use the shortest solution chamber (5 mm.) to bring the solutions within the concentration range of the instrument, even with this chamber it was necessary to dilute greatly the samples taken at the higher temperatures, since the maximum concentration directly measurable was 0.25 molal. In general, the samples were diluted to approximately the same concentration and calibration values were redetermined from time to time for this region to insure as accurate results as possible with the method employed.

4. **Freezing-Point Lowering and Eutectic Temperature.**—Exceedingly accurate determinations of the freezing-point lowering of aqueous solutions of mannite have been made by L. H. Adams[2] and also by R. E. Hall and W. D. Harkins.[3] The former found that the difference between the observed and calculated freezing-point depression is not greater than 0.0001° for concentrations of 4.02 to 62.59 millimols per 1000 g. of water. E. H. Loomis[4] made freezing-point measurements over a wider range of concentrations, using the Beckmann method; the difference between the observed and calculated[5] depression for a solution containing 206.1 millimols per 1000 g. of water is —0.0013°, the observed value being less than that calculated, contrary to the usual experience.

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[1] This Journal, **37**, 1181 (1915).

[2] *Ibid.*, **37**, 481 (1915).

[3] *Ibid.*, **38**, 2668 (1916).

[4] *Z. physik. Chem.*, **32**, 599 (1900).

[5] Calculated from the equation $\Delta t_F = 103.20 (x_1 + 0.428 x_1^2)$, Washburn's "Principles of Physical Chemistry," 1915, p. 173, McGraw-Hill Co., New York.

In the present investigation the determination of the eutectic temperature and a freezing point between the eutectic and 0° was made. To determine the latter, the zero reading of the Beckmann thermometer was first determined by placing it in a mush of pure water and ice contained in a Dewar tube in the apparatus already described. A portion of the water was replaced by a solution of mannite previously cooled to 0°, and having approximately the concentration required for the desired depression. When the temperature became constant, a sample was withdrawn through the alundum filter, properly diluted and then analyzed. To determine the eutectic temperature most of the mannite solution was removed from the Dewar and replaced by a cooled saturated solution together with a large excess of mannite crystals. The mixture was well stirred but did not attain constant temperature for several hours, when a sample of the equilibrium mixture was withdrawn and its composition determined. The data are given in the following table:

Concentration moles per 1000 g. of water	Freezing point depression observed	Freezing-point depression calculated[1]	Difference observed-calculated
0.2709	0.505°	0.501°	0.004°
0.5460	1.019° (eutectic)	1.009°	0.010°

The figures in the fourth column show that the deviation from the calculated value is significant with solutions of high concentration and that the deviation is a function of the concentration.

5. Solubility Measurements.—In determining the solubility at and near 25°, 4 different procedures were tried: (1) water contained in a Dewar tube was saturated with mannite at 35–40° and cooled with stirring to the final temperature; (2) water at 25° was added to a large excess of crystals and frequently stirred for several hours; (3) water was added to a large quantity of crystals in a bottle and shaken in a thermostat at 25° for 24 hours; (4) same conditions as in (3) except that the solution was initially saturated at 40°. The results of these experiments are:

Procedure	Temperature Degrees	G. solubility of mannite per 100 g. of water.
(1).	24.9	21.48
	25.0 (interpolated)	21.57
(2).	25.2	18.66
(3)	25.0	21.54
(4)	25.0	21.63

It is quite evident that procedure 2 cannot be employed. Methods 3 and 4 are known to give the best results but require a long time. Procedure 1 may be employed since it yields results similar to those of the standard methods and, moreover, it possesses the advantage of requiring but a short time.

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[1] Washburn, $\Delta t_F = 103.20 (x_1 + 0.428 x_1^2)$, "Principles of Physical Chemistry," 1915, p. 173, McGraw-Hill Co., New York.

The procedure in all solubility determinations between 50° and 90° was essentially the same The solution was saturated at a temperature about 10° higher than that at which the determinations were to be made, cooled to approximately 3° above the desired temperature, and then poured into a Dewar tube which was surrounded by an oil bath electrically heated and the contents mechanically stirred In the determinations between 90 and 103° it was usually found impossible to draw the samples for analysis into the flask in spite of all precautions, since the solutions were very concentrated and consequently highly sensitive to temperature change A column of liquid about 14 cm in length was usually obtained in the withdrawal tube before solidification occurred, the tube was then removed and cooled to completely solidify the contents The middle portion of the tube was cut off the contents dissolved in warm water and the final solution analyzed in the usual manner The weight of the sample was determined from the difference in weight of the glass tubing before and after removing the contents

It was the original intention to determine the solubility at 125 and 150° but it was found impossible to obtain a mixture at those temperatures which could be sampled In attempting to obtain the solubility at 125°, mannite was added to a boiling solution but the highest temperature reached at which the solution possessed even a medium degree of fluidity was about 110°. At this temperature water vapor was given off rapidly, resulting in the solidification of the solution. In an endeavor to obtain a solution at 150°, mannite crystals were melted and boiling water grad-

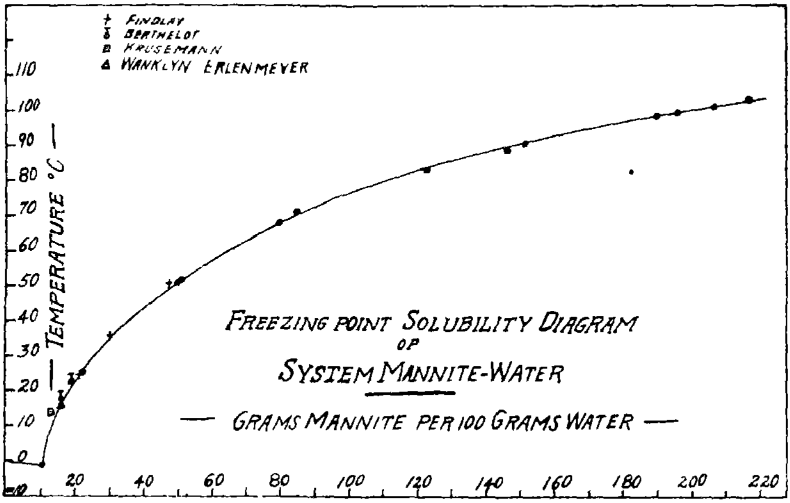

Fig 2

ually added. Most of the water immediately vaporized The addition of water caused a cooling of the liquid mannite and solidification of the entire mass resulted. To investigate the composition of solutions at these temperatures, therefore, pressure apparatus would be necessary.

The results of the solubility determination are given in Table I

TABLE I

Temperature Degrees	G of mannite in 100 g of water (weights *in vacuo*
1.019	9.942
25.00	21.63
25.00	21.57
50.70	49.0
51.50	49.9
67.4	78.6
70.5	83.0
82.9	121.0
88.1	145.5
90.1	150.6
98.0	189.0
99.3	195.0
100.8	200.0
101.8	206.0
103.6	216.0

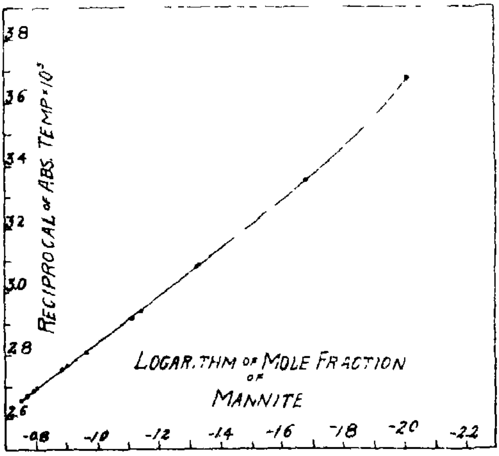

Fig 3

A large scale graph of these data was constructed in the form shown by Fig. 3. The data given in Table II were derived from this curve and present the results in a more convenient form.

TABLE II

Temperature Degrees	Solubility g of mannite in 100 g of water.	Mole fraction of mannite in solution
−1.019 (eutectic)	9.942	0.0097
0.00	10.36	0.0101
5.00	11.9	0.0117
10.00	13.7	0.0134
15.00	16.0	0.0156
20.00	18.6	0.0181
25.00	21.6	0.0209
30.00	25.2	0.0243
40.00	34.6	0.0331
50.00	47.6	0.0450
60.00	64.4	0.0598
70.00	86.2	0.0785
80.00	115.0	0.1019
90.00	150.0	0.1294
100.00	197.0	0.1633

Although the curve in Fig. 3 is not a perfectly straight line, the deviation does not indicate the presence of hydrates. Fig. 2 shows the freezing point-solubility diagram of the system mannite–water. The experimental difficulties in obtaining accurate measurements of the solubility near 100° were quite great and, consequently, the results in this region are somewhat uncertain. To complete the solubility curve for normal pressure a determination of the composition of the boiling saturated solution would be necessary.

V. Other Physical Properties.

In connection with this investigation the literature was carefully searched for data on physical properties other than those already mentioned. These data have been briefly summarized in the following sections:

1. **Density.**—All of the references to the density of mannite are old and do not contain sufficient information as to the conditions under which the measurements were made. Kruseman[1] obtained the values 1.4589 and 1.3938 at 0° and 50°, respectively, for purified crystalline mannite. Prunier[2] found the density to be 1.51 at 13°. He used a specific gravity flask with ether as the contact liquid but did not state what form the mannite was in. Several determinations were made by Schroder[3] on mannite in the form of coarse crystals and also of finely powdered material, using the displacement method with benzene as the contact liquid. His results are: 1.489 on a powdered sample of purified mannite, "Karlsruher Sammlung;" and 1.486 on Kahlbaum's crystals. The density is referred to water at 4° but the temperature was not stated. His values are undoubtedly the most dependable of the three.

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[1] *Ber.*, **9,** 1468 (1876).

[2] *Bull soc. chim.*, Paris, **28,** 556 (1877)

[3] *Ber* , **12,** 562 (1879)

2. **Specific Heat.**—Three investigators have determined the specific heat of mannite, using two somewhat different methods. Hermann Kopp[1] employed the method of observing the heat effect produced when a known quantity of mannite, covered by a liquid in which it was not soluble, was heated to a definite temperature and then immersed in a calorimeter. He obtained the value of 0.324 calorie per degree for a temperature range of 0–100°. Using essentially the same procedure, M. W. Longuinine[2] obtained as the average of 5 determinations the value 0.3277 calorie per degree for the temperature range 28–100°. W. F. Magie[3] determined the specific heat over a relatively short temperature range, using an apparatus primarily designed for very accurate measurements of the specific heats of solutions. He obtained the value 0.315 calorie per degree over the range 14–26°, with a possible error of 2 or 3%.

3. **Heat of Combustion.**—The heat of combustion of mannite was determined by Berthelot and Vieille,[4] using an oxygen bomb calorimeter. It was also determined by Stohmann and Langbein[5] who made two series of measurements, the last being on mannite recrystallized from alcohol several times, using a bomb calorimeter designed for very accurate work. The several results follow:

Berthelot and Vieille	Stohmann and Langbein	
(1887)	(1885)	(1892)
3 9997 Cal /gram	3 949 Cal /gram	3 9959
	3 922	4 0046
3 9928	3 946	3 9944
	3 947	3 9982
4 0110	3 940	3 9961
Av., 4 0012	3 941	3 9978

4. **Heat of Dilution.**—Measurements of the heat of dilution[6] of aqueous mannite solutions have shown, as would be expected, that only a slight evolution of heat occurs on dilution and that it is practically independent of the temperature.

VI. Summary.

The following physical properties of mannite and its aqueous solutions have been studied: The melting point of pure mannite, the specific rotation in aqueous solution, the freezing point-solubility diagram up to 103°. A brief summary of previous work on the subject has been given.

Since certain physical constants of mannite given in handbooks are not in accord with the best data, the following values based on results of the present investigation and on the most dependable results given in the literature are suggested for adoption: melting point, 166.05°; specific rotation $[\alpha]_D^{20°} = -0.244° \pm 0.002$ and $[\alpha]_D^{25°} = -0.208 \pm 0.002$ (calculated), density 1.48₇ (room temperature), specific heat $C_{(28-100°)} = 0.327_7$ cal./deg. and $C_{(14-20°)} = 0.31$ cal./deg., heat of combustion, 4.00° cal./gram.

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[1] *Trans. Roy. Soc. London*, **155**, I, 71 (1865).

[2] *Ann. chim. phys.*, **27**, 144 (1892).

[3] *Phys. Rev.*, **14**, 193 (1902); **17**, 105 (1903).

[4] *Ann. chim. phys.*, [6] **10**, 456 (1887).

[5] *J. prakt. Chem.*, [2] **31**, 291 (1885); **45**, 305 (1892).

[6] F. R. Pratt, *J. Frank. Inst.*, **185**, 663 (1918).

The writer wishes to acknowledge his indebtedness to Dr. E. W. Washburn under whose direction this investigation was made.

URBANA, ILLINOIS.

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, UNIVERSITY OF MINNESOTA.]

THE CALCULATION OF THE TEMPERATURE COEFFICIENT OF THE DISTRIBUTION RATIO.

BY F. H. MACDOUGALL.

Received July 10, 1919.

The present communication owes its origin to a recent paper[1] by Forbes and Coolidge dealing with the system water, ether and succinic acid and contains some new relations between various functions of the variables of ternary systems not contained in their article and, in particular, new additional relationships between the various partial derivatives to be defined later. The authors determined the composition of a large number of solutions both unsaturated and saturated with respect to various components. They use the following system of symbols:

s = mole fraction of succinic acid in water layer.
e = mole fraction of ether acid in water layer.
w = mole fraction of water acid in water layer.
σ = mole fraction of succinic acid in ether layer.
ω = mole fraction of water acid in ether layer.
ϵ = mole fraction of ether acid in ether layer.

The distribution ratio is $R = s/\sigma$ and the temperature coefficient is

$$\frac{dR}{dt} = \frac{1}{\sigma}\frac{ds}{dt} - \frac{s}{\sigma^2}\frac{d\sigma}{dt} = \frac{1}{\sigma}\left(\frac{ds}{dt} - R\frac{d\sigma}{dt}\right)$$

The authors put $\left(\frac{ds}{de}\right)_t = a$, $\left(\frac{ds}{dt}\right)_e = b$, $\left(\frac{de}{ds}\right)_t = m$, and $\left(\frac{de}{dt}\right)_s = n$. Then since $\frac{ds}{dt} = \left(\frac{ds}{dt}\right)_e + \left(\frac{ds}{de}\right)_t \frac{de}{dt} = b + a\frac{de}{dt}$ and $\frac{de}{dt} = \left(\frac{de}{dt}\right)_s + \left(\frac{de}{ds}\right)_t \frac{ds}{dt} = n + m\frac{ds}{dt}$ they obtain $\frac{ds}{dt} = \frac{b + an}{1 - am}$. Similarly they obtain $\frac{d\sigma}{dt} = \frac{\beta + \alpha\nu}{1 - \alpha\mu}$, where $\alpha = \left(\frac{d\sigma}{d\omega}\right)_t$, $\beta = \left(\frac{d\sigma}{dt}\right)_\omega$, $\mu = \left(\frac{d\omega}{d\sigma}\right)_t$ and $\nu = \left(\frac{d\omega}{dt}\right)_\sigma$.

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[1] THIS JOURNAL, 41, 150 (1919).

They thus arrive at the following relationship for the temperature coefficient $\frac{dK}{dt} = \frac{b + an}{\sigma(1 - am)} - \frac{s}{\sigma^1}\left(\frac{\beta + \alpha\nu}{1 - \alpha\mu}\right)$

Now, at first glance, the reader is surprised to see $\left(\frac{ds}{e}\right)_t$ put equal to a and $\left(\frac{de}{ds}\right)_t$ put equal to m and not equal to $\frac{1}{a}$ The reason of course is that the two derivatives in question refer to different curves representing different series of solutions Otherwise $1 - am$ would equal zero and so would $(b + an)$ equal zero and the ratios would be indeterminate It seemed to the present writer worth while to put the mathematical relations on a clearer and more definite basis so that the student might see at once the particular set of solutions or the particular curve to which each partial derivative refers With that end in view let us adopt the following scheme of symbols for the ternary system water, ether and succinic acid

Water Layer.

s_1 = mole fraction of acid in water layer, saturated with acid but not with ether

e_1 = mole fraction of ether in water layer, saturated with acid but not with ether

s_2 = differs from s_1 in that the solution is saturated with ether but not with acid

e_2 = differs from e_1 as s_2 differs from s_1

s_s and e_s refer to acid and ether in solutions saturated with both.

Ether Layer.

σ_1 and ω_1 = mole fractions of acid and water, respectively, in ether layer saturated with acid but not with water

σ_2, ω_2, σ_s, ω_s have meanings which are almost self evident

We have the following functional equations $s_1 = f_1(t,e_1)$ and $s_2 = f_2(t,e_2)$, represented at a fixed temperature, t, by two curves which intersect at a point where s_1 and s_2 become s_s and e_1 and e_2 become e_s. We can express these results as follows $s_s = \mathop{\mathrm{Lim}}\limits_{e_1 = e_s} f_1(t\,e_1) = \mathop{\mathrm{Lim}}\limits_{e_2 = e_s} f_2(t,e_2) = f_3(t) = f_4(e_s)$. Similarly we could write $\sigma_1 = \varphi_1(t,\omega_1)$, $\sigma_2 = \varphi_2(t,\omega_2)$ and $\sigma_s = \mathop{\mathrm{Lim}}\limits_{\omega_1 = \omega_s} \varphi_1(t,\omega_1) = \mathop{\mathrm{Lim}}\limits_{\omega_2 = \omega_s} \varphi_2(t,\omega_2) = \varphi_3(t) = \varphi_4(\omega_s)$ And finally,

$$\frac{ds_s}{dt} = \mathop{\mathrm{Lim}}\limits_{\substack{s_1 = s_s \\ e_1 = e_s}}\left(\frac{ds_1}{dt}\right) = \mathop{\mathrm{Lim}}\limits_{\substack{s_2 = s_s \\ e_2 = e_s}}\left(\frac{ds_2}{dt}\right).$$

Now from the 4 equations (only two of which are independent)

$$\frac{ds_1}{dt} = \left(\frac{ds_1}{dt}\right)_{e_1} + \left(\frac{ds_1}{de_1}\right)_t \frac{de_1}{dt}$$

$$\frac{ds_2}{dt} = \left(\frac{ds_2}{dt}\right)_{e_2} + \left(\frac{ds_2}{de_2}\right)_t \cdot \frac{de_2}{dt}$$

$$\frac{de_1}{dt} = \left(\frac{de_1}{dt}\right)_{s_1} + \left(\frac{de_1}{ds_1}\right)_t \cdot \frac{ds_1}{dt}$$

$$\frac{de_2}{dt} = \left(\frac{de_2}{dt}\right)_{s_2} + \left(\frac{de_2}{ds_2}\right) \cdot \frac{ds_2}{dt}$$

we obtain for the point at which the aqueous solution is saturated with both acid and ether,

$$\frac{ds_s}{dt} = \underset{e_1 = e_s}{\text{Lim}} \left(\frac{ds_1}{dt}\right)_{e_1} + \underset{e_1 = e_s}{\text{Lim}} \left(\frac{ds_1}{de_1}\right)_t \cdot \frac{de_s}{dt} =$$

$$\underset{e = e_s}{\text{Lim}} = \left(\frac{ds_2}{dt}\right)_{e_2} + \underset{e = e_s}{\text{Lim}} \left(\frac{ds_2}{de_2}\right)_t \cdot \frac{de_s}{dt}$$

$$\frac{de_s}{dt} = \underset{s_1 = s_s}{\text{Lim}} \left(\frac{de_1}{dt}\right)_{s_1} + \underset{s_1 = s_s}{\text{Lim}} \left(\frac{de_1}{ds_1}\right)_t \frac{ds_s}{dt}$$

$$= \underset{s_2 = s_s}{\text{Lim}} \left(\frac{de_2}{dt}\right)_{s_2} + \underset{s_2 = s_s}{\text{Lim}} \left(\frac{de_2}{ds_2}\right)_t \cdot \frac{ds_s}{dt}{}^{1}.$$

If we write the last 4 equations as follows·

$$\frac{ds_s}{dt} = b_1 + a_1 \frac{de_s}{dt} = b_2 + a_2 \frac{de_s}{dt}$$

$$\frac{de_s}{dt} = n_1 + m_1 \frac{ds_s}{dt} = n_2 + m_2 \frac{ds_s}{dt}$$

the meaning of the symbols a_1, b_1, n_1, m_1, etc., will be evident. For example $a_1 = \underset{e_1 = e_s}{\text{Lim}} \left(\frac{ds_1}{de_1}\right)_t$ and $a_2 = \underset{e_2 = e_s}{\text{Lim}} \left(\frac{ds_2}{de_2}\right)_t$, etc. Note that $a_1 = \frac{1}{m_1}$, $a_2 = \frac{1}{m_2}$, $n_1 = \frac{-b_1}{a_1}$, $n_2 = \frac{-b_2}{a_2}$.

From the equations we can get the following relations:

$$\frac{ds_s}{dt} = \frac{b_1 + a_1 n_2}{1 - a_1 m_2} = \frac{b_2 + a_2 n_1}{1 - a_2 m_1} = \frac{a_2 b_1 - a_1 b_2}{a_2 - a_1}$$

$$\frac{de_s}{dt} = \frac{n_1 + m_1 b_2}{1 - a_2 m_1} = \frac{n_2 + m_2 b_1}{1 - a_1 m_2} = \frac{b_1 - b_2}{a_2 - a_1}$$

An additional result such as $\frac{ds_s}{dt} = \frac{b_1 + a_1 n_1}{1 - a_1 m_1}$ is meaningless since the fraction is of the form $\frac{0}{c}$. In the same way we can obtain for the ether layer,

$$\frac{d\sigma_s}{dt} = \frac{\beta_1 + \alpha_1 \nu_2}{1 - \alpha_1 \mu_2} = \frac{\beta_2 + \alpha_1 \nu_1}{1 - \alpha_2 \mu_1} = \frac{\alpha_2 \beta_1 - \alpha_1 \beta_2}{\alpha_2 - \alpha_1}$$

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[1] Only the first two of these 4 equations are independent The four are written down to show the relationship to the results obtained by Forbes and Coolidge.

$$\frac{d\omega_s}{dt} = \frac{\nu_1 + \mu_1\beta_2}{1 - \alpha_2\mu_1} = \frac{\nu_2 + \mu_2\beta_1}{1 - \alpha_1\mu_2} = \frac{\beta_1 - \beta_2}{\alpha_2 - \alpha_1}$$

where the Greek letters have meanings for the ether phase, analogous to the Roman letters for the aqueous phase. Written in the above manner, there is no chance of mistaking the curve to which the partial derivatives refer. We readily see that in our notation,

$$\frac{dR}{dt} = \frac{1}{\sigma_s}\left(\frac{a_2b_1 - a_1b_2}{a_2 - a_1} - R.\ \frac{\alpha_2\beta_1 - \alpha_1\beta_2}{\alpha_2 - \alpha_1}\right)$$

or if we retain some of the letters, n_1, n_2, m_1, m_2, etc., we obtain the expression

$$\frac{dR}{dt} = \frac{1}{\sigma_s}\left(\frac{b_1 + a_1n_2}{1 - a_1m_2} - R.\ \frac{\beta_1 + \alpha_1\nu_2}{1 - \alpha_1\mu_2}\right)$$

identical, of course, with the one given by Forbes and Coolidge when the proper interpretation is given to the letters used by them.

MINNEAPOLIS, MINN.

RELATIONS BETWEEN DISTRIBUTION RATIO, TEMPERATURE AND CONCENTRATION IN SYSTEM: WATER, ETHER, SUCCINIC ACID.

By G. S. Forbes and A. S. Coolidge

Received July 23, 1919

F. H. MacDougall, in the preceding article, points out the possibility of misunderstanding the physical significance of certain partial derivatives in our paper as published in THIS JOURNAL.[1] He shows how confusion may be rendered impossible by use of a more elaborate set of symbols. On page 161 of our article directions are given for finding the derivatives by drawing tangents to the intersecting curves in Fig. 3 and reading the slopes. The values given for the slopes will identify the derivatives beyond question even if doubt previously existed concerning them. We are glad to note that Professor MacDougall agrees with our final conclusion.

CAMBRIDGE, MASS.

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[1] 41, 150 (1919)

[CONTRIBUTION FROM DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NORTH CAROLINA.]

ZIRCONYL COMPOUNDS WITH THE OXY-HALOGEN ACIDS.[1]

By F. P. Venable and I. W. Smithey.

Received July 23, 1919.

Little is known of the zirconyl oxy-halogen salts though a chlorate, iodate, and periodate have been mentioned in the literature. The following investigation was undertaken to devise methods of preparation, to see if definite compounds could be obtained, and also to observe the effects of hydrolysis upon them. The salts prepared were those with iodic, perchloric, and chloric acids.

Zirconyl Iodate.

As zirconium hydroxide is insoluble in iodic acid this salt was prepared by precipitation. When a concentrated solution of iodic acid is added to one of zirconyl chloride a curdy, white precipitate forms immediately. As the solution is added gradually the precipitate first forms, redissolves on stirring, but soon becomes permanent. The precipitate settles readily and can be washed by decantation. A similar precipitate forms when an alkali iodate is substituted for iodic acid, which, according to Brinton and James,[2] is almost insoluble in nitric acid, provided a considerable excess of the iodate ion is present. Davis[3] states that the precipitation with an alkali iodate added in excess, is almost quantitative but, on account of the varying composition of the precipitate it could not be used analytically.

The precipitate formed was a white powder, insoluble in water, alcohol, and ether. It was decomposed by conc. hydrochloric acid with evolution of chlorine. It showed decomposition when heated to 100° and iodine vapors were distinctly visible at 125°. For analysis, therefore, samples partially dried at room temperature were used. Five preparations were made, care being taken to have neither compound in excess in the precipitation. In the first preparation both solutions were concentrated and the iodic acid added gradually to the zirconyl chloride. In the remaining preparations more dilute solutions were used to make handling the precipitates easier. In the first and second preparation no additional water was used for washing, but the water present, which should contain practically only hydrochloric acid, was removed so far as possible by suction. The third preparation was washed with 6 liters of water at room temperature in one-liter portions. The fourth preparation was treated with 20 liters of hot water in one-liter portions, and the fifth in the same way with 30 liters of hot water. It was thought that this change of conditions should give an approximate idea as to the progress of hydrolysis. The analyses were made by treating the sample with conc. hydrochloric acid and titrating the liberated chlorine with sodium thiosulfate. From the hydrochloric acid solutions thus obtained the zirconium hydroxide was precipitated by ammonium hydroxide, ignited, and weighed as zirconia.

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[1] Submitted to the Faculty of the University of North Carolina by I. W. Smithey as part of the requirement for the degree of Master of Science.

[2] THIS JOURNAL, **41**, 1080 (1919).

[3] *Am. Chem. J.*, **11**, 26 (1889).

In reporting the analyses and calculated formulas the following considerations have prevailed with us. The hydrolyzing of zirconium salts results in the formation of zirconyl compounds and the separation of the acid radical which, if soluble, is removable by water. The zirconyl salt is commonly hydrolyzable further, resulting in the separation of more of the acid radical and the formation of a basic zirconyl compound. In the case of the chloride this hydrolysis may proceed until comparatively little of the acid radical is left. The question then arises as to the composition of the basic radical. The normal hydroxide is quite unstable and the methods of preparation used in the investigation would seem to preclude its presence in the basic compounds. The facts of ionic dissociation give abundant evidence of the existence of the ZrO radical in such compounds and, according to some investigators, of the existence also of another radical, Zr_2O_3. We have been chiefly influenced by the fact that dialysis separates zirconyl hydroxide from strongly hydrolyzed solutions and prefer to regard these basic compounds as addition compounds with zirconyl hydroxide and the use of such formulas undoubtedly presents a better picture of the progress of the hydrolysis. There is evidence also that part of the water is more persistently retained.

Analyses of the compounds to be described in this paper were made in duplicate. Only one is reported unless there were noteworthy variations in the duplicates or other reasons make it advizable to give both.

1. Precipitate formed from concentrated solutions and unwashed so that the first stage of hydrolysis might undergo no change. The analyses on the water free basis yielded the ratio $ZrO : IO_3 :: 30.62 : 69.38$. The formula $ZrO(OH)_2.2ZrO(IO_3)_2$ gives the ratio 31.36 : 68.64.

2. Precipitated from more dilute solutions and unwashed to observe the effect, if any, of change in concentration. With more time at disposal a series of experiments with measured changes of concentration would have been carried out. From the analyses on water free basis the ratio $ZrO : IO_3 :: 33.14 : 66.86$ was obtained. The ratio calculated for $5ZrO(OH)_2.8ZrO(IO_3)_2$ is 33.11 : 66.89. The amount of water then in the solutions materially affects the degree of hydrolysis.

3. The preparation made as in No. 2 was washed with 6 liters of water at room temperature to observe the effect of cold water upon the precipitate already formed. The water was used in one-liter portions. The analyses (water free) gave the ratio $ZrO.IO_3 :: 34.73 : 65.27$. The formula $3ZrO(OH)_2.4ZrO(IO_3)_2$ would require $ZrO.IO_3 :: 34.76 : 65.23$.

4. The preparation was washed with 20 liters of boiling water in one liter portions to test the effect of increased amount of water and raised temperature. The ratio

found here was $ZrO:IO_3::48.33:51.67$, and that required for the formula $2ZrO(OH)_2.ZrO(IO_3)_2$ is $47.75:52.25$.

5. The preparation was washed with 30 liters of boiling water in one-liter portions to magnify such effects as might be caused under the conditions in No 4 The analytical results gave the ratio $ZrO:IO_3::55.38$ 44 62 For the formula $3ZrO(OH)_2 ZrO(IO_3)_2$ the ratio is 54.92:45.08 The hydrolysis, therefore, has progressed still further.

Whether the analyses are to be taken as representing definite compounds or not is not very material for our purposes. It might possibly be settled by repeating the experiments under identical conditions to see whether the same compounds were always obtained. The iodate offers many advantages on account of its insolubility and quantitative precipitation for studying this and other points, and such work may be done later. For the present it remains to sum up the results obtained under a few rather arbitrary, widely-varying conditions, as follows:

No.	Conditions of precipitation.	Formulas		Mols. hydrolyzed per 1000
		With H_2O	Without H_2O	
1	Pptd from conc sol ; unwashed .	$ZrO(OH)_2 2ZrO(IO_3)_2$	$Zr_3O_4(IO_3)_4$	334
2	Pptd. from dil sol , unwashed	$5ZrO(OH)_2 8ZrO(IO_3)_2$	$Zr_{13}O_{18}(IO_3)_{16}$	385
3	Pptd. from dil sol ; washed; cold H_2O	$3ZrO(OH)_2 4ZrO(IO_3)_2$	$Zr_7O_{10}(IO_3)_8$	431
4	Pptd. from dil sol , washed; 20 liters boiling H_2O	$2ZrO(OH)_2 ZrO(IO_3)_2$	$Zr_3O_7(IO_3)_2$	667
5	Pptd. from dil sol , washed, 30 liters boiling H_2O	$3ZrO(OH)_2 ZrO(IO_3)_2$	$Zr_4O_7(IO_3)_2$	750

The normal zirconyl iodate $ZrO(IO_3)_2$ is not formed by this method but, if formed, is immediately more or less hydrolyzed. At some later time efforts will be made to prepare both this and the normal iodate.

Zirconyl Perchlorate.

This compound has not been previously prepared. The ordinary 60% perchloric acid showed little solvent power, but on diluting with an equal amount of water it dissolved zirconium hydroxide readily. Bearing in mind the influence of temperature upon hydrolysis two different methods of solution were used. In the first case cold diluted acid was allowed to stand in contact with an excess of the hydroxide for some weeks. The clear liquid was then separated from the undissolved hydroxide and allowed to evaporate over calcium chloride. Two large crystals and several smaller ones formed. The larger ones measured 15 × 14 × 11 mm. and 13 × 12 × 9 mm., respectively, and apparently belonged to the triclinic system. They weighed over 2.5 g. each after drying between filter paper, and were analyzed. The zirconium hydroxide was precipitated by ammonium hydroxide, washed and ignited for zirconia. The filtrate and washings, containing ammonium perchlorate, were evaporated on a water bath, dried, weighed, and analyzed on a water-free basis.

Calc for $4ZrO(ClO_4)_2.ClO_4H$ ZrO_2 32 20 ClO_4, 67 65 Found ZrO_2 (1), 31 52, (2), 32 11, ClO_4 (1), 68 48, (2), 67 80

The second method of preparation was by heating the perchloric acid with an excess of zirconium hydroxide on a water bath until no more hydroxide was dissolved This saturated solution formed, on cooling, radiating clusters of crystals from which individual crystals could not be separated. The mother liquor was poured off, the crystals washed with a small amount of water and placed over sulfuric acid They were very deliquescent and failed to dry completely They were odorless, soluble in alcohol, ether, benzene, chloroform, and carbon tetrachloride, but no crystals were obtained from these solutions A small portion heated quickly on platinum foil exploded with a sharp report, but when heated slowly it intumesced, leaving finally a white mass of zirconia. Decomposition was evident at 100° Four different preparations were made and samples analyzed with the following results

Water free ZrO_2 37 79, 37 84, 37 82, 37 70 ClO_4 62 21, 62 16, 62 18, 62 30

The reaction, then, may be represented by the equation

$$8ZrO(ClO_4)_2.ClO_4H + 2ZrO(OH)_2 = ZrO(OH)_2.9ZrO(ClO_4)_2 ,$$

two molecules of the zirconyl perchloric acid dissolving two molecules of zirconyl hydroxide, this being the limit of saturation The percentages required by the formula for this basic zirconyl perchlorate on the water-free basis are ZrO_2, 37 32 and ClO_4, 62 68 The crystalline character of the product and the uniformity of the results from several different preparations would go to show that the compound is a definite one We have in these two compounds analogy with zirconyl sulfuric acid, $ZrOSO_4.SO_4H_2$

In attempting to purify by recrystallization the crystalline crop obtained on saturating perchloric acid with zirconyl hydroxide it was found that, while crystals formed, they had returned to the composition of the original zirconyl perchloric acid, $4ZrO(ClO_4)_2.ClO_4H$ Part of preparation No. 1 was recrystallized 4 times and of preparation No 2, 5 times, and the resulting crystals analyzed

Found ZrO_2 (1) 31 77, (2) 32 31 ClO_4 (1) 68 23, (2) 67 69

These results agree with those required for the formula $4ZrO(ClO_4)_2.ClO_4H$.

This would appear to be the more stable form, two molecules of it having the power of forming a compound with one molecule of zirconyl hydroxide, this being dissociated on resolution

Zirconyl Chlorate.

Weibull[1] has reported the preparation of this compound by the double decomposition of zirconium sulfate and barium chloride according to the equation

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[1] *Art Univ. Lund*, II, 18 V, 53 (1881)

$$Zr(SO_4)_2 + 2Ba(ClO_3)_2 = BaSO_4 + Zr(ClO_3)_4,$$

assigning to the product the latter formula. Details and analyses are not given. Zirconium sulfate, however, is hydrolyzed in solution and the chlorate cannot well have the composition indicated as it also hydrolyzes.

Basic zirconyl chlorate was prepared by us by adding a solution of potassium chlorate to a cold concentrated solution of zirconyl perchlorate. An abundant crop of crystals formed immediately, consisting of potassium perchlorate and containing no zirconium. Additional crops of these crystals were separated as evaporation proceeded, the mother liquor becoming yellow, syrupy, and smelling of chlorine dioxide. Further concentration yielded larger, well formed crystals, differing from the preceding crops. Only a faint test for potassium was obtained. The crystals were very deliquescent, soluble in alcohol but insoluble in ether. They had a slightly yellowish color and oxidized organic matter. Some of the crystals were washed and dried over phosphorus pentoxide. Neither calcium chloride nor sulfuric acid were effective as drying agents. In analyzing the chlorine was determined by dissolving a weighed amount in water in a small flask fitted with a separatory funnel for hydrochloric acid, a tube for admitting carbon dioxide, and a delivery tube connected with two U tubes in series, containing potassium iodide solution. The liberated iodine was titrated with 0.1 N sodium thiosulfate. The zirconium hydroxide was precipitated from the hydrochloric acid solution, ignited, and weighed. Two preparations were analyzed on a water free basis.

Calc. for $ZrOOH.3ZrO(Cl$[illegible] ZrO 45.06; ClO 54.[illegible]. Found ZrO_2, (1) 45.18, (2) 45.95; ClO [illegible] 54.[illegible], [illegible] 54.[illegible]

The normal zirconyl chlorate was therefore not obtained. If formed, it was hydrolyzed under the conditions of the experiment. The hydrolysis is less far reaching than in the case of the iodate, as only one out of four of the molecules are hydrolyzed compared with one out of three in the latter case. The definite nature of the hydrolyzed product is proved by the crystalline form. It is manifestly not very stable, as shown by the liberation and decomposition of chloric acid.

Summary.

1. Several basic zirconyl iodates were prepared and the stages of progressive hydrolysis indicated.

2. The perchlorate $4ZrO(ClO_4)_2.ClO_4H$ was obtained. This can be dissolved and recrystallized without further hydrolysis. Two molecules of it when warmed will dissolve two molecules of zirconyl hydroxide, forming $ZrO(OH)_2.9ZrO(ClO_4)_2$, which is also crystalline. On redissolv-

ing and crystallizing the acid perchlorate or zirconyl perchloric acid separates.

3. The basic zirconyl chlorate formed is crystalline and corresponds to the formula $ZrO(OH)_2.3ZrO(ClO_3)_2$. It is easily decomposed.

CHAPEL HILL, N. C.

[CONTRIBUTION FROM THE KENT CHEMICAL LABORATORY OF THE UNIVERSITY OF CHICAGO.]

STUDIES IN CONDUCTIVITY. V. NOTES ON THE MEASUREMENT OF THE CONDUCTIVITY OF SOLUTIONS.

BY H. I. SCHLESINGER AND F. H. REED.[1]

Received July 28, 1919.

During the past few years a series of very thorough and valuable papers by Washburn and his associates[2] on the methods and apparatus for measuring the conductivity of solutions has been published. Other papers by Acree and his students[3] have also added greatly to our knowledge of the subject. Nevertheless a number of difficulties which we have encountered in the measurements required for our work on formic acid solutions have either not been touched on at all or have received only very scant attention as will be pointed out below. Since we have developed simple criteria for detecting the difficulties in question and simple methods for overcoming them, it has been suggested to us that the publication of a résumé of these points would be of value to other workers in this field.

The resistance of the solutions was measured by the Wheatstone-Kohlrausch method, using a Siemens and Halske high frequency generator, a rotary bridge, and a standardized Curtis coil resistance box. The connections and the methods of shielding the apparatus are those recommended by Washburn and Bell.[4] In conjunction with the high frequency circuit we used a Leeds and Northrup condenser which permits of placing equal capacities in series with the two lines of the circuit; by means of a two-way switch this condenser could be eliminated and readings taken without any capacity in the high frequency circuit. It was observed that the introduction of the condenser, while it improved the sharpness of the minimum, decidedly shifted its position and that the shift thus produced depended on the type of resisting medium and the magnitude of the resistance. The shift was particularly large when the usual Wheatstone bridge set-up, that is with the current entering at the ends of the bridge, was used. Thus, the introduction of the condenser did not shift the minimum when a resistance coil of approximately 300 ohms was measured against 300 ohms in the Curtis box, but with 400 ohms the minimum shifted from 0.5001 to 0.5005, and when a 1000 ohm coil was measured against a 1000 ohm Curtis coil from 0.5001 to 0.5013. It is seen therefore that when the type of the resisting medium remains the same the shift in the minimum increases with the resistance to be measured. But there is another factor involved, for when the coil resistance is replaced by a cell containing 0.01 *N* solution of potassium chloride, larger shifts are obtained even with smaller resistances. Thus in a cell in which the solution had a resistance of approximately 880 ohms, the bridge reading shifted from 0.2540 to 0.2589 with the condenser, while in another cell in which the resistance of the same solution was 1387 ohms, the reading shifted from 0.2238 to 0.2320. It is to be noted that even where the shift is very large, each reading was very sharp, the maximum error of setting being not greater than 0.0001

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[1] The work reported in this and the following paper of this series has been presented to the Faculty of the Ogden Graduate School of Science of the University of Chicago by F. H. Reed in part fulfillment of the requirements for the degree of Doctor of Philosophy. The work was completed in the fall of 1916.

[2] THIS JOURNAL, 38, 2431 (1916); 39, 235 (1917).

[3] Acree and Taylor, *Ibid.*, 38, 2396 (1916).

[4] THIS JOURNAL, 35, 177 (1913). An excellent résumé of the Washburn apparatus is given in the Leeds and Northrup *Catalog* 48 (1915).

It is of course necessary to eliminate such shifts. To do this we first determined the arrangements of the bridge, etc., which gave correct readings when two standardized Curtis coils (each of 1000 ohms) were placed in the two remaining arms of the bridge, and it was found that the results without capacity in the high frequency circuit were correct, whereas the use of the condenser produced the sort of shift described. In order to retain the advantages of having resonance on the circuit, and at the same time to avoid the difficulty described, we investigated the matter from an experimental point of view and found the following: (1) The shift could be completely eliminated by having capacities in the two sides of the circuit which were not identical. When, for example, the two capacities were, respectively, 0.0245 and 0.0225 microfarad, the shift was greatly decreased but not entirely eliminated. No further changes in capacity which could be produced by our Leeds and Northrup condenser made further improvement, but by using a small variable Clapp-Eastham air condenser in parallel with the smaller capacity we eliminated the divergence for all cases investigated. The setting of this condenser for our purpose made the total capacity for this side about 0.0228 microfarads. There is, however, a disadvantage in using this method of avoiding the difficulty; for when the capacities are adjusted to give correct readings for the case in which the shift is fairly great, the setting is also correct for any case where the divergence is smaller, but not necessarily so where it is greater. This condition necessarily leads to uncertainty in the results. (2) It was further found that when the bridge was arranged to have the telephone at the ends of the slide wire the shift was very much reduced. We shall call this arrangement "set-up A" while the arrangement usually used is called "set-up B." Thus, in the case in which with set-up B the bridge reading with equal capacities was 0 2320 and without capacity was 0 2238, the corresponding readings were 0 2234 and 0.2238, respectively, for set-up A, and where set-up B gave smaller shifts than this, set-up A gave identical results with, or without, capacity. Furthermore, in the case of set-up A, when the capacities in the high frequency circuit were 0 0245 and 0 0225, respectively, instead of equal, the introduction of the condenser into the circuit no longer produced any shift in the minimum and gave the correct reading for every type and value of resistance measured by us Small changes, such as would be produced by introducing the air condenser, have no effect on the readings with set-up A. This arrangement has, however, the disadvantage that a larger amount of current flows through the cell than with set-up B, and more heating of the solution results This difficulty can be completely overcome by making an approximate setting, waiting until the solution returns to the bath temperature, and then making the final reading very quickly. It is also helpful to use a resistance in the box somewhat smaller than the resistance in the solution [1]

The explanation of the results described can doubtless be found in some dissymmetry in the high frequency circuit[2] before it reaches the bridge. We were unable to locate it and made no extended efforts to do so as we eliminated the difficulty by the method described. The reason why set-up A gives smaller deviations than does set-up B is probably because the arrangement of the bridge in the former is more nearly symmetrical and consequently produces more nearly equal energy losses in the various arms of the bridge.

There is another source of possible error in measuring resistances of solutions which has not received the attention which it deserves in the treatment of the subject. In the papers to which reference is made above the fact that the minimum may be perfectly sharp and yet may not be correct has been mentioned, but no stress has been laid on this important point. Acree, for example, has stated that one of the criteria for the reliability of a cell is that it must give for the ratio of the resistance of two solutions measured in it the same value as is found in some other cell. This may be put in other words by the statement that the cell constant must be the same no matter what standard solution is used to determine it. It is of course the usual procedure to determine the cell constant with more than one solution. But more than this is necessary to make certain that the cell in question is suited to the solutions whose conductivities are to be determined in it. It is essential that the standard solutions used to determine the cell constant have in the cell a range of resistance completely covering the range of the solutions to be measured in it. That this is not usually understood is demonstrated by the fact that the specific conductivities determined by Kohlrausch, which are usually employed as standards for the determination of cell constants, are not well enough distributed to cover satisfactorily every possible range of resistance. The data presented below will make this point clear.

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[1] That the readings as usually taken by us and the readings at the center of the bridge give identical results, with the set up used, was repeatedly proven. We also found that the capacity of approximately 0 024 microfarads in the condenser was the amount required to produce resonance, and that making the capacities in the two sides of the circuit unequal did not materially decrease the current obtained

[2] That the difficulty did not lie in an inequality of the capacities of the two sides of the condenser was shown by a rough measurement of the capacities and by substituting two standardized capacities for the one we had been using

In previous work on anhydrous formic acid a special form of Arrhenius cell, with fixed electrodes, adapted to the measurement of fairly dilute solutions, has been employed.[1] These cells have cell constants of approximately 0.2, as determined with both 0.02 N and 0.01 N solutions of potassium chloride. Since these cells are not well adapted to the measurement of concentrated solutions, without the use of fairly large capacities in parallel with the bridge circuit, no further determinations of the cell constants were made at that time as the only other Kohlrausch standards are fairly concentrated solutions. The more accurate measurements of the formate solutions required for the work to be reported in later papers gave reason to doubt the reliability of these cells and measurements of the cell constant with a larger number of solutions were carried out. For this purpose we used 0.01, 0.02, 0.05 and 0.2 N solutions of potassium chloride and made the equivalent conductivities of A. C. Melcher, reported in the paper of Noyes and Falk,[2] the basis of the calculation of the cell constant. The data obtained for one of these "Arrhenius type" cells as well as for the two cells referred to by the symbols H_1 Fig. 1, and H_3 are given in Table I. The latter are cells of the kind which have been constructed for the later work on formic acid solutions. Their construction will be sufficiently clear from Fig. 1 The electrodes are platinized. The cells are particularly well adapted to work where only a small volume of solution is available since 20 cc. of solution brings its level so high above the electrodes that the addition or removal of 1 cc. or slight tilting of the cell does not change the observed resistance. Furthermore, the

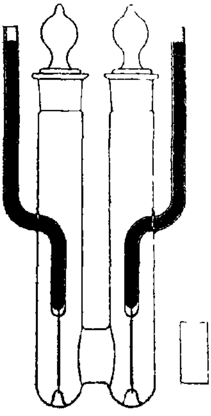

Fig. 1.

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[1] This Journal, 36, 1589 (1914)

[2] *Ibid.*, 34, 454 (1912).

readings are very sharp over wide ranges of concentration and only small capacities are required in parallel with the bridge circuit in order to obtain excellent minima.[1] Throughout a period of more than a year in which the cells were constantly in use the cell constants did not change, which shows that the support for the electrodes is sufficiently rigid. In the table mentioned above, the solutions used, the measured resistance (*R*) in ohms and the cell constant (*C*), calculated from the latter for each of the 3 cells are given. The resistances are in each case the averages of very closely agreeing duplicates made with different solutions prepared from different samples of potassium chloride which had been recrystallized several times from conductivity water with all due precautions and had then been ignited.

TABLE I

The Variation of Cell Constant with Increasing Resistance of the Solution in the 'Arrhenius' Cell

KCl solution	Arrhenius cell		Cell H1		Cell H3	
N	*R*	*C*	*R*	*C*	*R*	*C*
0.01	142.38	0.2015	1391.1	1.9684	883.37	1.2501
0.05	30.25	0.2021	294.49	1.9682	187.12	1.2506
0.2	8.21	0.2040	79.25	1.9686	50.35	1.2509
0.02	72.77	0.2018	710.40	1.9707	451.21	1.2517

Leaving out of consideration for the moment the results obtained with the 0.02 *N* solution, we see that the cell constant of Cell H1 does not vary and that the variation in Cell H3 is only 0.06%. Hence we may conclude that we may use H3 for solutions whose resistance in the cell lies between 79 and 1400 ohms and H_3 for resistances between 50 and 880 ohms. As a matter of fact, it is only the lower limit which is of importance. For some reason, which we are unable to explain, the 0.02 *N* solutions give divergent results, the only suggestion which we can offer is that there may be an error in the equivalent conductivity reported by Noyes and Falk. If we now examine the data for the "Arrhenius" cell we see that the cell constant undergoes an apparent change of over 1% in the same range of concentrations which gave a maximum variation of only 0.06% in the other cells, even although each reading in the "Arrhenius type" cell was very sharp, quite as sharp in fact as in the other cells. It is clear, therefore, that the "Arrhenius" cell is not adapted to the whole range of resistance covered by these solutions, although there is nothing in the individual readings to indicate this fact. The following data show, furthermore, that although the cell constant may be the same when calculated from the results obtained with solutions of different concentration the cell may, nevertheless, not be satisfactory unless the standard solutions cover the correct range of resistance. In the cells H1 and H3, the average of the ratio of the resistance of the 0.01 *N* to that of the 0.02 *N* potassium chloride solution is 1.9580. In the "Arrhenius" cell the ratio is 1.9566, which differs from the one obtained in the other cells by only 0.07%. In other words, the cell constant of the "Arrhenius" cell calculated from the resistance of the 0.01 *N* solution would differ hardly at all from that calculated from the resistance of the 0.02 *N* solution and the unreliability of the cell would have been overlooked had only these two solutions been used.[1]

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[1] In the "Arrhenius type" cells, for example, a capacity of 0.18 microfarad had to be used in parallel with the bridge circuit to obtain a good minimum for small resistances, while for the type of cell here described the maximum capacity required for our solutions was less than 0.01 microfarad.

Summary.

It has been pointed out that even though the minima obtained in the measurement of the resistance of solutions by the usual method may be perfectly sharp, the results may nevertheless be incorrect and criteria for determining the reliability of the measurements and methods for overcoming some of the difficulties encountered have been suggested.

CHICAGO, ILL.

[CONTRIBUTION FROM THE WOLCOTT GIBBS MEMORIAL LABORATORY OF HARVARD UNIVERSITY.]

CONCENTRATED THALLIUM AMALGAMS: THEIR ELECTROCHEMICAL AND THERMOCHEMICAL BEHAVIOR, DENSITIES AND FREEZING POINTS.

BY THEODORE W. RICHARDS AND FARRINGTON DANIELS.

Received August 1, 1919.

More than twenty years ago a series of investigations on the thermodynamics of amalgams was begun in Harvard University.[2] Recently, similar investigations have been conducted by G. A. Hulett.[3] The further interesting contributions of Joel H. Hildebrand concerning the vapor pressure of amalgams have added important auxiliary information.[4]

Nevertheless, the complete understanding of the electrochemical, thermochemical, and osmotic performance of these interesting metallic solutions has not been attained. This is unfortunate, since the nature of amalgams renders them more susceptible to varied investigation than that of many other types of solutions. It might reasonably be hoped that knowledge gained from these might be transferred by analogy to other solutions, even to aqueous ones, as regards those aspects of solution not involving electrolytic dissociation.

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[1] Errors of the kind found in the case of the "Arrhenius" cells are doubtless due to polarization.

[2] T. W. Richards and G. N. Lewis, *Proc. Am. Acad.*, 34, 87 (1898); T. W. Richards and G. S. Forbes, *Carnegie Inst. Publications*, 56, 1 (1906); T. W. Richards and J. H. Wilson and R. N. Garrod-Thomas, *Ibid.*, 118, 1 to 72 (1908); T. W. Richards and F. Daniels, *Trans. Am. Electrochem. Soc.*, 22, 343 (1912).

[3] G. A. Hulett and DeLury, THIS JOURNAL, 30, 1805 (1908).

[4] J. H. Hildebrand and E. D. Eastman, *Ibid.*, 36, 2020 (1914); 37, 2452 (1915).

Therefore it seemed to be worth while to follow further possible lines of investigation suggested by earlier researches in the hope of attaining a satisfactory solution of the points not yet completely understood. For this purpose thallium lends itself more advantageously than any common metal possessing a moderate solution tension, because thallium is extraordinarily soluble in mercury. Even at 20° the liquid amalgam may contain as much as 43.3% of thallium. Such amalgams give sharp and constant values for their single potentials in aqueous solutions of thallous salts. Hence the free energy of transfer of thallium from one to another of these amalgams can be determined with great accuracy.

Bearing these facts in mind, about 8 years ago we began an extended research upon both concentrated liquid and solid thallium amalgams, using both electrochemical and thermochemical methods. The experimental part of the research, which was to supplement the earlier work of one of us with J. H. Wilson on dilute thallium amalgams, was completed in the spring of 1914, but its publication has been delayed partly by the desire to correlate more fully the varied results, and partly by other pressing duties, occasioned by the great war. The work involved the determination of electromotive forces at several temperatures, densities, heat capacities, heats of solution of thallium in mercury, heats of dilution of the amalgams, melting points of solid amalgams, and allied problems. The several details are recorded below, together with some of the conclusions which may be drawn from the facts. The discussion of the theory is best postponed until the facts have been presented, since the method of attack was inductive rather than deductive. A more complete interpretation, which attempts to present a consistent theory of the constitution of the amalgams, and indicates the general tendencies at work in all such systems, will be the subject of a later communication.

The Purification of Materials.

The thallium material came from different sources, some from pure metallic thallium of commerce, some from earlier pure amalgams, and some from older residues purified by precipitating as iodide, converting into the nitrate, and precipitating impurities with hydrogen sulfide. A slight residue left after the solution of metallic thallium in strong sulfuric acid was filtered off and discarded, and the excess of acid was driven off by heating. The fused cake of thallium sulfate from all sources dissolved completely in water. The salt was once crystallized, and its solution then allowed to stand in porcelain for a week or more with occasional stirring, in contact with pure electrolytic metallic thallium. After filtration of this solution, the salt was 3 times crystallized, being drained each time with a small efficient centrifuge.

Pure thallium was prepared by electrolysis of a solution of this sulfate and pure ammonium oxalate, using platinum electrodes. Thallium peroxide persistently formed on the anode, although conditions were varied over a wide range. An electrolyte made by mixing equal parts of saturated solutions of each salt, with a moderate current density, was the most satisfactory. A piece of chemically clean cotton cloth tied around the anode of platinum foil kept the peroxide from gaining access to the cathode. From time to time the thallium collecting on the cathode was removed, washed, and preserved in pure water in contact with another platinum cathode (3 volts), and thus preserved from oxidation The electrolysis was continued until a portion of the solution showed only a slight turbidity with potassium iodide. The thallium was then thoroughly washed, although it was found impossible to remove the last trace of salt, as shown with either barium acetate or potassium iodide. After being pressed into small porcelain boats, the metal was fused in a current of hydrogen in a porcelain tube, and kept in dry glass bottles. Of course it oxidized slightly on the surface, but before weighing it was carefully scraped clean and bright. Because of its manner of preparation it may have contained a trace of sulfide, but this was probably removed and accounted for during amalgamation.

Crude mercury, after long contact with conc. sulfuric acid, was dropped in a fine stream several times through a solution of mercurous nitrate and dil. nitric acid, and then distilled in a current of air under reduced pressure, as recommended by Hulett.[1] Mercury thus prepared can hardly contain any impurity except dissolved oxygen. In order to eliminate this possibility, the metal was redistilled in a current of purified hydrogen, and sealed under hydrogen in a glass bulb, provided with a stopcock. Subsequently the mercury was kept and used wholly out of contact with air. Oxygen, which is fatal to accurate measurement of this kind must have been excluded.

Ammonium oxalate used for the electrolysis of thallium was made from oxalic acid and ammonium hydroxide. A strong solution of oxalic acid (58%) was brought to boiling, filtered and strongly acidified with redistilled hydrochloric acid. After cooling and recrystallizing 3 times, the chloride was found to have been removed. The oxalic acid was neutralized with concentrated, freshly distilled ammonia, and the resulting ammonium oxalate was 3 times recrystallized. More ammonia was added as needed to replace that driven off by heating.

Distilled water was redistilled from alkaline permanganate solution and again from a few drops of sulfuric acid, using block tin condensers.

All the hydrogen used was generated from pure zinc and hydrochloric acid,[1] and was purified and dried by passing over a strong solution of caustic potash on glass pearls, and through two towers containing fused potassium hydroxide. Rubber tubes were avoided, and in this apparatus sealed glass connections everywhere effectually excluded air from the hydrogen.

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[1] *Z. physik. Chem.*, 33, 611 (1900); *Phys. Rev.*, 21, 388 (1905).

The Preparation of the Amalgams.

The method of making amalgams used by Richards and Wilson[2] was first employed. Thallium was electrolytically deposited in pure mercury, the concentration being calculated from the weight of silver deposited in a coulometer in the same circuit.

By a method of analysis to be described presently it was found that although dilute amalgams may be made fairly accurately in this fashion, concentrated amalgams always contained less thallium than the quantity corresponding to the current and time. This is doubtless due to the diffusion of dissolved oxygen or thallic sulfate from the anode to the neighborhood of the cathode after the current has been running a few minutes. No matter how carefully the electrolyte is at first freed from oxidizing material, it must very soon be impregnated with it. Accordingly the electrolytic method was later abandoned, and the amalgams were made separately, by mixing actually weighed amounts of mercury and thallium. The amalgamation of each piece of the metal was effected with the help of a few cc. of dilute standard acid, which dissolved the superficial trace of oxide on the thallium.[3] The amalgamation was conducted in a closed test tube, into which projected a very finely pointed, small pipet arranged essentially in the fashion adopted in the electrolytic method. The mixing was completed by bubbling hydrogen through the amalgam. Precautions against the presence of air are not very important at this stage, since allowance would be made for oxidation by means of the acid titration which immediately followed. The remaining acid was immediately titrated with standard alkali (using methyl orange), and the weight of thallium present in the aqueous solution was calculated and subtracted from the weight of thallium taken. The end-point was accurately determined and the correction (which never amounted to more than a few milligrams) for the dissolved thallium must have been accurate to within 0.1 or 0.2 mg. The only uncertainty lay in a doubt as to the exact composition of the trace of oxidized film on the surface of the metal at the time of weighing, but when large quantities are taken this uncertainty is negligible, especially since thallium has so large an equivalent.

When the amalgamation and mixing were complete (and before the titration of the supernatant acid), the homogeneous liquid amalgam was almost all drawn into the small pipet which had previously delivered the gas. When the amalgam has been almost wholly withdrawn from the test tube, the suction was stopped, hydrogen was admitted above, and the pipet was removed for immediate discharge into the electrolytic cell in which it was to be measured.

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[1] The generator used is described in *Carnegie Inst. Publications*, 56, 10 (1906).

[2] *Carnegie Inst. Publications*, 118, 9, 10, 11 (1909).

[3] Richards and Forbes, *Carnegie Inst. Publications*, 56, 18 (1906). The trace of sulfide, if present, was probably also dissolved.

The advantages of this procedure over the former method of Richards and Wilson are several. Large bulbs and stopcocks need not be put on the balance, and weighings may be made accurately to tenths of a milligram. Each amalgam was made up separately and a possible error in one concentration would not be repeated in the others. Hence the absolute average values are safer. The mixing by bubbling hydrogen gas was more efficient than could be caused by the gentle rocking of the cell. The manipulation was simpler and more rapid, and with pure materials ready, the amalgams could be made, the cell filled, and measurements taken at different temperatures, all in one day—a distinct advantage when the amalgams may change in composition on standing a long time under the electrolyte, as in this case. On the other hand, the new method lacks the consistency as regards relative measurements which is attained by making all of the amalgams from a single "parent" amalgam. This last circumstance was that which determined the procedure in the work of Richards and Wilson.

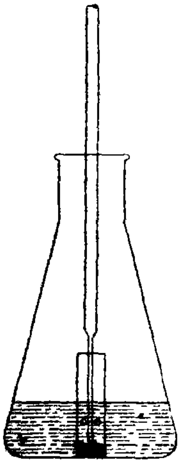

Fig. 1.—Apparatus for preparing thallium amalgams for volumetric analysis.

In order to test the concentration of these and other thallium amalgams, a convenient method of volumetric analysis was devised which proved to be accurate, simple, and rapid, and may find application in other work. The sample of amalgam, which should contain about 0.2 g. of thallium, is accurately weighed, placed in a 100 cc. Erlenmeyer flask, and covered with 50 cc. of standardized 0.02 *N* sulfuric acid. A short piece of wide, glass tubing is fitted snugly over the globule of amalgam to hold it in place, and a long capillary tube is inserted under the metal so that pure air may be bubbled through it and cause rapid oxidation. Two small holes blown near the bottom of the larger tube aid in the circulation of the acid (Fig. 1). The thallium is oxidized and the oxide at once dissolves in the sulfuric acid, which is too dilute to attack the mercury as long as any thallium remains. The end-point of the oxidation may be estimated readily from the behavior of the mercury, since, when the thallium has been removed, the agitation due to the air causes the formation of a great number of small globules which will not unite again, probably because of a very thin, unweighable film of mercurous sulfate. Subsequent bubbling fails to diminish the concentration of the supernatant acid. When the small globules thus no longer unite to form larger ones, the flask is removed and the excess of acid titrated with exactly standardized alkali. To make sure that all the thallium has been oxidized, one cc. of acid is added and air bubbled through for an hour more. If the alkali then required is not equivalent to the added acid, the removal of thallium has not at first been complete, and the process must be repeated until there is no loss. Another trial is rarely necessary. The time required varies with the rate of bubbling and the adjustment of the tube from perhaps 2 to 10 hours, but the procedure requires no attention. Methyl orange or methyl red may be used as an indicator. The best results are of course obtained if the end-point is judged by comparison with indicator in thallium sulfate solution or in a properly prepared buffer solution. The accuracy of the method may be gathered from the results shown in Table I. The first 3 results were obtained in 1912 and the rest in 1913, using a new standard solution.

TABLE I

Comparison of Methods of Determining Composition

Amalgam	By titration %	By direct weighing %	Error %
A	21.70	21.722	0.10
B	13.07		
	13.09	13.128	0.37[1]
C	4.936	4.930	0.12
D	10.02		
	10.01	10.019	0.04
E	42.93	42.858	0.13

The Thermostats.—Two thermostats were used, one at 30°. The other, containing two regulators, could be set either at 20° or at 40°. They were electrically heated, constant within 0.01°, and thoroughly stirred.

The Cell.—The amalgams were contained during the electrical measurements in the 4-cupped glass vessel used previously in this laboratory[2] and shown in the diagram (Fig. 2). It has an advantage over the later modification of Hulett's,[3] in that larger amounts of amalgam may be used without danger of accidental mixing, and therefore slight losses due to possible oxidation are robbed of much of their injurious effect.

In a cell composed of dilute and concentrated amalgam, both lose thallium by oxidation, but the dilute amalgam loses a larger percentage of its contents than the concentrated one, in a given time, since the oxidation is more rapid than the diffusion of dissolved oxygen. Hence the electromotive force of the cell rises. On this account not only was air scrupulously excluded, but all the measurements were made as quickly as possible. Although in early measurements trouble was experienced from oxidation, in the later ones it was adequately excluded, as is shown by the following two series of measurements, the first made immediately after the preparation of the amalgams, and the second after 9 days·

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[1] With the exception of the doubtful case B, the volumetric results were accurate within 0.1 or 0.2 mg of thallium with the weights taken. This degree of accuracy is not of the same order as the high accuracy of the potential measurements, but it affords nevertheless a useful check on the results

[2] Richards and Forbes, *Carnegie Inst. Publications*, 56, 22 (1906)

[3] Hulett and De Lury, THIS JOURNAL, 30, 1814 (1908).

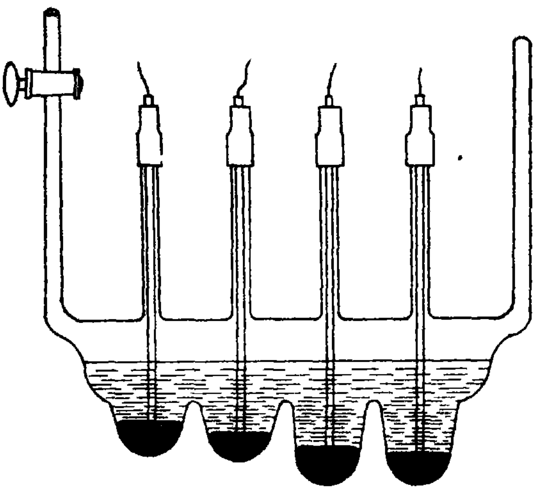

Fig. 2. Cell with amalgams.

TABLE II

Constancy of Measurements

	20°	1-2	2-3	3-4
I	April 15	0.011572	0.008681	0.008174
II.	April 24	0.011574	0.008681	0.008175

Concentrations, %

1 = 20.970, 2 = 27.362, 3 = 34.029, 4 = 42.858

The precautions needful to attain such a result are so important that they follow in detail.

The multiple cell was fused to the hydrogen generator, and after having been evacuated and filled with hydrogen several times it was almost filled with the electrolyte—a solution (about 2%) of the purest thallium sulfate in freshly distilled water. The solution had been boiled, cooled in pure hydrogen, subjected to a continuously bubbling stream of this gas (in order to remove dissolved air), then drawn into a hydrogen-filled finely pointed pipet, provided with a stopcock, and finally sealed off in hydrogen. From this pipet the filling of the cell was conducted through one of the projecting tubes of the latter in the presence of a counter current of hydrogen, the other tubes being closed. As a further precaution, the cell was subsequently evacuated and the solution was allowed to boil under reduced pressure, all of the 4 projecting tubes being closed by short lengths of cleaned pressure tubing and glass rods.

When all was ready, the several amalgams were introduced into their respective cups as rapidly as possible. The capillary jet of a pipet was inserted into one of the rubber tubes of the glass cell until the point extended below the surface of the electrolyte, in such a position as to be free from the danger of introducing any amalgam into the wrong cup. On the withdrawal of the pipet, the platinum wire (protected by glass) for making electrical connection was immediately substituted, the hydrogen stream continuing. Thus in rapid succession the 4 cups were filled, and the cell was ready for electrical measurement. The copper wires making connection with the potentiometer joined the platinum in mercury contacts beneath the level of the thermostat; hence thermoelectric effects were excluded.

The Potentiometer.—The potentiometer was that used in the earlier investigation by Wilson and Garrod-Thomas, already mentioned, but for the final readings it was adjusted anew and several improvements were made tending toward the elimination of parasitic electromotive forces. This instrument and all the rest of the measuring apparatus was shielded by a grounded equipotential shield[1] of copper, the various parts of the potentiometer being mounted on separate glass plates held firmly in place on the shield with paraffin The heavily insulated copper wires forming the connections were enclosed in glass tubes. The binding posts as well as connectors were of solid copper, and contacts between unlike metals were reduced to a minimum. The potentiometer was covered by a large glass case in which a small fan (rotated by a distant electric motor) kept all parts at uniform temperature. The rocker switches and bridge rider were operated by cotton strings from a considerable distance.

The thermostat was found sometimes to be the seat of parasitic effects. When it was insulated, these effects were greatly magnified. Accordingly the water in the thermostat, and the relay, were grounded, whereupon this trouble disappeared. Too much emphasis cannot be put upon this precaution with regard to electrically heated thermostats.

The arrangement thus mounted permitted reading to one one-millionth of a volt. Sundry experiments were made in order to determine if its accuracy corresponded with this high degree of sensitivity. The agreement found by measuring separately several cells and comparing the sum of the separately measured electromotive forces with the actually measured total value of all in series was as good as could be expected. Such comparison is easily made in the 4-cupped cell employed. For example (in Series III at 30.00°), the cell I–L equalled 0.028945, whereas this value calculated as the algebraic sum of other combinations yielded, respectively, 7, 8 and 9 instead of 5 as the last figure, the other figures being the same. Thus the greatest deviation was 0 000004 volt, and the average could hardly be in error 0 000002 volt

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[1] W. P. White, *Phys. Rev.*, 25, 341 (1907); This Journal, 36, 2011 (1914).

TABLE III

Final Results (1913)

(Series III.)

E in Millivolts

	Concentration	20°	30°	40°
A	0 3315			
		45 550	46 937	48 326
B	1 704			
		26 395	27 050	27 704
C	3 768			
		9 763	9 968	10 168
D	4 935			
E	4 930			
		29 480	29 971	30 467
F	10 019			
		24 342	24 660	24 981
G	17 049			
		9 581	9 703	9 833
H	21 025			
I	20 970			
		11 572	11 741	11 915
J	27 362			
		8 681	8 844	9 001
K	34 029			
		8 174	8 360	8 547
L	42 858			
F	10 019			
		33 769	34 208	34 656
M	20 780			
		20 341	20 678	21 011
N	34 029			
		8 518	9 761	11 034
P	(49 418) Solid			
Q	10 30			
		32 360	32 791	
R	20 78			
		28 892	30 477	
S .	(49 48) Partly solid			
		2 5[1]	2 7[1]	2 8[1]
Tl	Pure Tl			
U .	(49 418) Partly solid Amalgam			
		—0 001	0 000	..
V	Amalgamated Tl			

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[1] These figures are only approximate The potential of pure thallium is being investigated further

Search was made for other possible disturbing conditions, however remote, which might be a source of error, but none was found. The room was usually very dry, and the introduction of a desiccating agent in the potentiometer case made no appreciable difference. The apparatus was never used in very humid weather, when, of course, electrical measurements are always difficult.

The Measurement of Amalgam Cells.—With amalgams and potentiometer prepared as described above, and with gradually increasing trustworthiness as the work proceeded, measurements were made during many months. As a rule, the readings were very definite and constant, although in a few cases shaking of the cell caused slight fluctuations in the electromotive force, dispelled by a few seconds' repose. Electrolytic metallic thallium, employed in one cell, in the form of a fine crystalline sponge, also gave a fairly constant potential.[1] Amalgamated thallium and solid amalgams at 20°, or above, gave electromotive forces fully as constant as those of the liquid amalgams. The solid amalgams of less than $33^1/_3\%$ at 0°, however, were not reproducible to millionths of a volt. The formation of mixed crystals may have introduced uncertainty here.

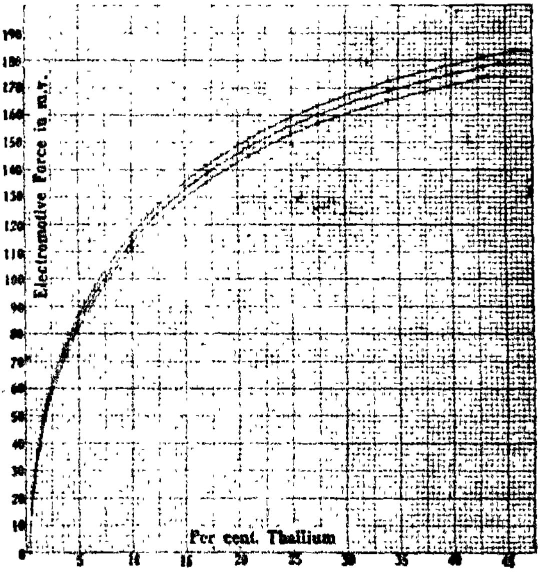

Fig. 3. Electromotive forces of amalgam cells at 20°, 30°, and 40°. Uppermost curve 40°.

The preliminary measurments need not be recorded here. One of them has already been published.[2] It is enough to say that they were essentially identical with the results on p. 1740.

The accompanying graph (Fig. 3) pictures the final series of determinations at 20°, 30° and 40°, the weakest amalgam of this series (0.3315%)

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[1] Richards and Lewis, *Proc. Am. Acad.*, 34, 87 (1898). Lewis and Brighton point out that this is particularly the case with soft metals such as lead. Thallium is even softer than lead. THIS JOURNAL, 39, 1906 (1917).

[2] Richards and Daniels, *Loc. cit.*

being taken as the starting point with zero potential. They all (even the preliminary determinations) fall on a perfectly smooth curve; the error of plotting on coördinate paper as large as 44 × 53 cm. is much greater than the experimental error. The work of Richards and Wilson, below 2%, also falls exactly on the curve.

When the saturation point of the liquid amalgam has been reached, excess of thallium is without effect on the potential; the curve breaks into a horizontal straight line at a point giving the concentration at which solid and liquid are in equilibrium. A 43.3% thallium amalgam, then, has a freezing point of 20.00°. Similarly, the freezing points at 30° and 40° correspond to 44.5 and 45.8%, respectively. The horizontal line in the diagram indicates, of course, the coexistence of two phases in equilibrium.

Electrolytic thallium gave a potential somewhat more negative (2.49 millivolts at 20°) than amalgamated thallium. In an entirely independent more recent investigation (as yet unpublished) of Grinnell Jones and W. C. Schumb on the single potential of the thallium electrode, almost identical results were found. On the other hand, Lewis and von Ende[1] assumed from the results of Kurnakow and Puschin and of Sucheni (stating that their own experiments corroborated these results) that no difference in potential between thallium and the saturated amalgam exists. This apparent discrepancy will receive detailed discussion in a later communication.

The potentials of the liquid amalgams as given above are far greater than those demanded by any method of expressing the simple concentration law. For example, the observed potential between amalgams F and G above at 30° is 24.66, whereas the formula $(RT/F)\, ln\, C_1/C_2$ demands 13.88 and the formula $(RT/F)\, ln\, (1 + N_2)/(1 + N_1)$ demands 13.91.[2] This great discrepancy is even more highly interesting and important than the other. It will receive detailed consideration in the theoretical paper to which reference has already been made.

The Temperature Coefficient of the Cells and the Equation of Helmholtz.

The data in the table just given afford exact means of calculating the temperature coefficients of the several cells, and therefore of applying the equation of Helmholtz to them and calculating their heat effects.

The column before the last gives a quantity (the temperature coefficient of the potential of the cell divided by E_0, potential at 0°) which should equal the coefficient of expansion of a perfect gas, if the potential were due entirely to the concentration effect. The values of E_0 as far as the 17% amalgam could have been actually measured, but the amalgams containing over 17% of thallium partly crystallized at 0°. In all cases the valves of E_0 were found by extrapolation from those at 20° and 40°. The minimum in this column at about 19% is very marked and is undoubtedly significant. Evidently the temperature coefficient is much less than that demanded by the gas law.

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[1] G. N. Lewis and von Ende, THIS JOURNAL, 32, 732 (1910).

[2] See Richards and Daniels, *Loc. cit.*; Richards and Wilson, *Ibid.*, page 63; and Hildebrand and Eastman, *Ibid.*, p. 2456.

TABLE IV

Temperature Coefficients and the Helmholtz Equation

Conc	$\Delta E/\Delta T$ (20–30°).	$\Delta E/\Delta T$ (30–40°)	$\Delta E/\Delta T$ (Average)	$\Delta E/E_0 \Delta T$ 20–40°	U (joules)
0.3315	0.0001387	0.0001388	0.0001388	0.00325	470
1.704	0.0000656	0.0000654	0.0000655	0.00261	696
3.788					
	0.0000205	0.0000201	0.0000203	0.00215	370
4.935					
4.930					
	0.0000491	0.0000496	0.0000493	0.00173	1449
10.019					
	0.0000318	0.0000321	0.0000319	0.00135	1445
17.049					
	0.0000122	0.0000130	0.0000126	0.00135	568
21.025					
20.970					
	0.0000169	0.0000174	0.0000172	0.00149	631
27.362					
	0.0000163	0.0000157	0.0000160	0.00191	386
34.029					
42.858	0.0000186	0.0000187	0.0000187	0.00238	261
0.3315–42.86	0.0003697	0.0003708	0.0003703		6276
34.029					
	0.0001243	0.0001273	0.0001258		
49.418 (solid)					
Solid Amalg		(0.00 20.00°)			
Pure Tl	0.0000179	0.0000142	0.0000160		

The values in the last column are calculated from the familiar equation of Helmholtz, as applied to a gram-atom of a univalent metal:

$$U = EF - FT\frac{\Delta E}{\Delta T}$$

They will be compared later with the actual values found thermochemically.

The agreement between the values at 20–30° and 30–40° is not perfect, since they represent small differences between large quantities; the temperature coefficient over the higher temperature range averages 0.28% higher than that over the lower range, and individual differences are in some cases much greater Nevertheless, probably most of the average values given in the fourth column (and therefore those in the fifth) are within 1% of the truth.

The Densities of Thallium Amalgams.

Since, as one of us, with the help of J. H. Wilson, had already shown, thallium expands appreciably on amalgamation, the densities of the amalgams were needed in the theoretical consideration. These were determined as follows:

An Ostwald-Sprengel pycnometer, holding 1.0911 cc., was used in determining the densities. Determinations were made at both 20° and 30°, thus giving the coefficient of expansion, and furnishing an approximate mutual check on the results.

TABLE V.

Densities of Thallium Amalgams.

I. Thallium %	II Obs density 20°	III Obs density 30°	IV Values from smooth curve 30°	V Average densities	VI Diff V–IV	VII Coeff of exp.
0.000	13.5463	13.5218	13.522	13.522	0.000	0.000181
0.331			13.514	13.516	0.002	
1.704[1]			13.484	13.493	0.009	
3.788			13.440	13.459	0.019	
4.930	13.439	13.415	13.415	13.439	0.024	0.000179
7.496[1]	13.383					
10.019			13.306	13.354	0.048	
17.040	13.190	13.167	13.167	13.237	0.070	0.000175
21.025	13.108	13.087	13.087	13.170	0.083	0.000161
21.16[1]			13.105			
27.362	12.980					
33.70[1]	12.854					
34.029	12.846	12.828	12.828	12.953	0.125	0.000140
39.702			12.715			
42.858	12.676	12.656	12.656	12.805	0.149	0.000157
44.30			12.629			

Wilson's determinations at 20° gave, for amalgams containing, respectively, 0.793, 1.410 and 1.854% of thallium, densities 13.527, 13.515 and 13.504, respectively—values which fall precisely upon our curve.

These densities are plotted in the accompanying graph (Fig. 4). The curves are almost rectilinear; their slight lack of parallelism is due to the change of the coefficient of expansion indicated in the last column. The dotted line in Fig. 4 records the values which the densities would have possessed if there had been no expansion on amalgamation, taking 11.85 as the density of pure thallium. Evidently the expansion on amalgamation is 1.05% of the total volume in the case of the 40% amalgam, and others in proportion.

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[1] Our early determinations (1912). All the others given in the table were made more accurately in 1913.

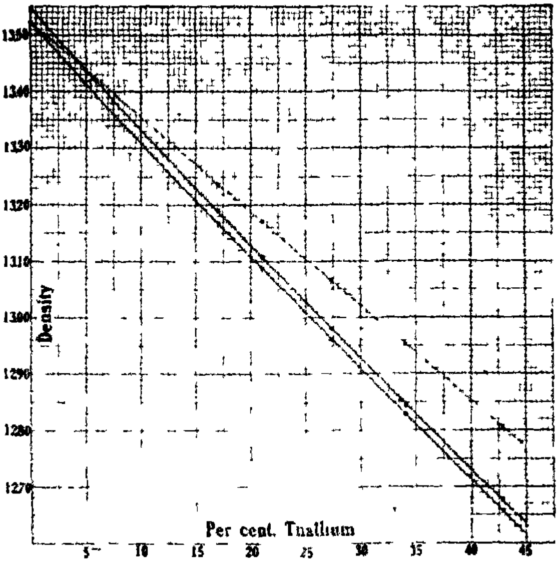

Fig 4.—Densities of thallium amalgams at 20° and 30°
Upper curve 20° Dotted line hypothetical.

The "solution volume"[1] of a gram-atom of thallium, *i. e.*, the excess in volume of an amalgam containing 204 g. of the solid metal over and above the volume of its mercury, is nearly independent of the concentration, varying only from 17.47, in the case of amalgams containing between 20 and 25% of thallium, to 17.51, in the case of very concentrated or very dilute amalgams. The following table exhibits the values at successive concentrations, the densities being taken from the smooth curve

Table VI

Solution Volume of Thallium in Mercury

(Sp Vol of Mercury at 30° = 0 073955 = V_0)

Per cent b	Density	Sp vol (V)	$\frac{100\ V}{b}$	$\frac{100-b}{b}V_0$	Sol vol 1 g Tl	Mol. sol. Vol
5	13 414	0 074549	1 49098	1 40515	0 08583	17.51
10	13 310	0 075131	0 75131	0 66560	0 08571	17 48
15	13 208	0 075712	0 50475	0 41908	0 08567	17 48
20	13 107	0 076295	0 38148	0 29582	0 08566	17 47
25	13 007	0 076882	0 30753	0 22187	0 08566	17 47
30	12 908	0 077471	0 25824	0 17256	0 08568	17 48
35	12 809	0 078070	0 22306	0 13735	0 08571	17.48
40	12 710	0 078678	0 19669	0 11093	0 08576	17 49

The values show a slight minimum at 22 5°, but otherwise, as already stated, are surprisingly constant Whether or not this minimum truly exists, or is only an outcome of slight experimental defect, could hardly be stated positively without further very exact experimentation with a larger pycnometer, for which time was lacking.

The coefficients of expansion are less constant; they show a distinct decrease with increasing concentration.

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[1] See Bousfield and Lowry, *Trans. Faraday Soc.*, 6, 85 (1910).

For further understanding of the situation, all the other thermal effects involved should also be carefully evaluated by experiment, including in addition to the temperature coefficient of the electromotive force (already detailed), the heat capacities and the heat of dilution of the several amalgams, and the heat of solution of thallium in mercury as well as in amalgams of increasing strength. These topics are considered in order below.

The Determination of Heat Capacities.

The procedure consisted in introducing a known quantity of heat into a weighed amount of amalgam and observing the rise in temperature. Electricity was passed through a heating coil of insulated manganin wire encircling the thermometer bulb in the amalgam, which was contained in a small adiabatic calorimeter, and the quantity of energy was determined by measuring the fall of potential across the coil and the quantity of electricity passing. The rise of temperature was measured on a sensitive thermometer. The calorimeter of the apparatus finally adopted and used with satisfaction for the determination of the heat capacities is shown diagrammatically in Fig. 5.

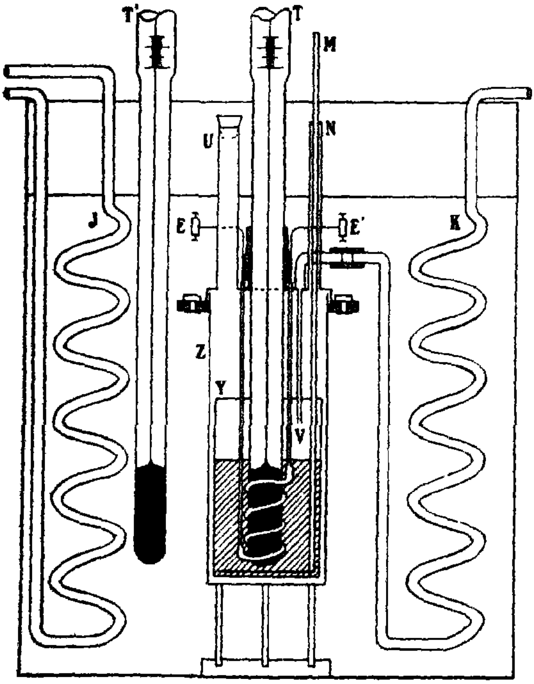

Fig. 5.—Calorimeter E, E', binding posts. J, K, coils of brass pipe. M, stirrer fitting in bearing, N. T, T', Beckmann thermometers. U, tube for removal of amalgam and introduction of mercury V, glass tube for entrance of carbon dioxide gas. Y, cylindrical brass can, surrounded by larger brass can, Z.

Thirty cc. of material from a special pipet was always taken for a determination. The substance to be measured was held in the cylindrical can Y, which was constructed of brass, 35 mm. in diameter and 51 mm. high. This fitted into a larger brass can, Z, and it was held in place by bits of cork, so that there [illegible] *everywhere* between the two cans, A cover of brass with a wide flange was clamped securely to a similar wide flange on the can by means of 4 screws (binding posts from dry batteries). Each flange had cemented to it with shellac a washer of pure, soft rubber. The surface of each washer was smeared with paraffin rubber, and when the cover was screwed down firmly, this arrangement gave an oil-tight closure. The outer can, thus equipped, was securely fastened in a glass battery jar which was filled by a thin paraffin lubricating oil. The accurate Beckmann thermometer T was fitted in a short, copper tube soldered to the center of the cover, and was held firmly in position by shellac and a ring of heavy rubber tubing. This gave a secure setting, but allowed a certain amount of flexibility. The thermometer registered 6° and was divided into 0.01°, so that 0.001° could be estimated. The manganin coil, completely encased in glass, encircled (without actually touching) the thermometer bulb; and its leads, also encased in glass, came through two holes in the cover to the binding posts E and E′. It was securely fastened to the cover by means of de Khotinsky cement, which proved to be admirably suited to the purpose, after other cements had been found wanting. The small tube N, soldered to the cover, extended up above the oil level and allowed the manipulation of a stirrer, M. This stirrer consisted of a flat, copper ring, slightly smaller in diameter than the inner can, fastened to a glass tube which served as a handle. The other tube, U, projecting above the surface of the oil, was for the removal of amalgam and the introduction of mercury. During the heat capacity measurements it was closed by a stopper.

Since brass and copper are readily attacked by mercury, the interior of the inner can and stirrer were covered with a thin coating of asphalt varnish and thoroughly dried. The mercury did not work through this and was not soiled by it. Neither shellac, paint, nor collodion met these requirements.

The amalgam was protected from oxidation by a persistent atmosphere of pure, dry carbon dioxide. The stream of gas which had passed through a spiral brass coil immersed in the oil bath was delivered above the surface of the amalgam by means of a small glass tube, V, containing a fine aperture at the end. There was no danger of loss or gain of heat by the amalgam on account of this gas, since the oil bath was kept at the temperature of the amalgam. A fine capillary insured a uniform rate of flow (about 30 bubbles through the wash-bottles in a minute) during the entire day. At night a bit of paraffin was melted around the only free opening, where the stirrer fitted into the tube N, so that the calorimeter was gas-tight and the carbon dioxide current was thereby stopped. The continuous outflow of gas around the stirrer effectually prevented any access of exterior air, which might have otherwise been pumped into the inner vessel by the stirrer, with accompanying contamination of the amalgam and gain or loss of heat.

A second Beckmann thermometer, T′, exactly like the first, was placed in the oil bath near the calorimeter. The two thermometers were carefully set, so that at 20° they were within 0.01°.

The oil was heated during an experiment by means of an electric current passing through ribbon composed of a suitable alloy. About 3.6 meters of this were wound in a spiral around a glass framework just inside the glass battery jar. This is not shown in the figure. It was connected with the alternating lighting circuit of 110 volts through a knife switch, a suitable permanent resistance and a rheostat in which each stop corresponded to a rise of temperature in the oil of about 0.01° per minute. Thus it was easy to arrange the rheostat so as to obtain a rise which kept pace with that of the calorimeter. The oil was kept thoroughly mixed by a rapidly agitated stirrer. After a determination was finished, the oil was cooled again, so as to be ready for the next experiment, by passing cold water through the coil of brass pipe, J. One hour was usually required before the thermometer in the amalgam fell from 25.0° back to 20°.

The current for heating the coil in the amalgam was furnished by the lead storage cell. It was connected with the leads of the inner heating coil through a delicate relay, a sliding resistance, and a knife switch. The relay (which was of very low ohmic resistance to minimize heating and consequent changing of the current in the circuit) controlled a stronger, entirely separate current actuating a device for releasing a stop watch, which was stopped by a spring the moment that the currents ceased to flow. Thus the duration of the current was automatically timed to within a fifth of a second. There was also an amperemeter, which served to give an approximate idea of the current. The sliding resistance consisted of a heavy manganin wire mounted on a glass bridge. A slider with a platinum point moved back and forth on it, so that the resistance in the circuit could be changed at will, thus regulating the fall of potential across the heating coil. It was found necessary to polish the manganin wire with chamois skin every day to insure a good contact.

The fall of potential across the terminals of the heating coil EE′ was measured by an Ostwald-Poggendorff potentiometer, which was fed by a cell of cadmium amalgam, dil. cadmium sulfate solution, mercurous sulfate and mercury. It was balanced against a standard cadmium cell by slipping one of its connecting wires of fine manganin wire back and forth in the binding post until there was no deflection of the galvanometer. This simple method of adjusting the potentiometer is very convenient and sufficiently accurate. The shunt of the potentiometer box was connected through the galvanometer and a knife switch with the terminals of the coil EE′. The reading on the potentiometer box (0.7612 volt, kept the same in any given series, so that calibration was not necessary) was of a magnitude suitable for bringing all the factors to about the same order of accuracy. The mirror-galvanometer was read by means of a suitably arranged spot of light, which could be seen readily from the experimenter's position. Manipulation of the sliding contact of the heating circuit kept the galvanometer reading very near zero throughout the determination, and hence maintained a constant electromotive force at the terminals of the heating coil.

The complete insulation of the quantitative heating coil EE′ of manganin wire was attained by enclosing it in a very thin glass tube. Upon this the success of the method was dependent. Several glass tubes were drawn out to capillaries until one was obtained which just slipped over the wire and fitted it snugly. The two were then carefully heated to a faint red heat and bent into a coil. The glass melted around the wire at the same time. This coil was soldered to leads of large copper wire, encased in glass tubes, and larger glass tubes were melted in place around the two connections.

Since the arrangement was precisely the same in each experiment, and the method was a strictly comparative one, the exact resistances of the manganin wire and copper leads need not be accurately known. Neither need the small fraction of the heat developed in the leads which was communicated to the calorimeter be determined. Nevertheless, the resistance of the manganin wire was measured, and found to be 1.224 ohms (constant over wide range of temperature), and that of the leads 0.004 ohm. Making due allowance for the resistances in the lead wires (0.004 ohm), the effective potential was found to be $\pi = 0.7587$ volt. Hence the constant π^2/r, to be multiplied by the time in seconds in order to obtain the energy in joules, was 0.47035. The result divided by the rise of temperature (always nearly 5.000°) gave the heat capacity of the system, from which the heat capacity of the calorimeter was subtracted. This was determined by means of sixteen independent experiments made upon pure mercury, which gave as the value of the heat capacity the value 72.40 mayers, with an average deviation of 0.04. With such a large number of results a close approximation to the true value must have been obtained.

Assuming (with Bartolli and Stracciati) the specific heat of mercury to be 0.03344 between 20° and 25°, the heat capacity of the calorimeter, thermometer, and fittings must have been $72.40 - 408.16 \times 0.03344 \times 4.178$[1] $= 15.37$ mayers. This value was used throughout the following work.

Having thus found the constant of the apparatus and attained facility

[1] The heat capacity of a gram of water at 22.5° in mayers

in its use, we proceeded to carry out precisely similar experiments upon thallium amalgams. Two series were made, in each case starting with a concentrated analyzed amalgam, and going step by step to more and more dilute ones. At each step some of the amalgam was carefully withdrawn and weighed, and about an equal weight of mercury (also carefully weighed) was added by means of a peculiar pipet to be described later. Thus the concentration of the amalgam at each step could be easily calculated. As a check upon the chain of operations, from time to time the portions withdrawn were analyzed,[1] and, moreover, at the conclusion of each series the actual weight of the most dilute amalgam was determined. These checks were entirely satisfactory, and afforded satisfactory evidence that no accidental gross error in weighing had been made at any stage.

The results with thallium amalgam follow, the average for the mercury being placed at the head of the table.

TABLE VII

Heat Capacities of Amalgams

Designation of amalgam	Thallium %	Weight G	Time Seconds	Temp rise °C	Total heat cap Mayers	Heat capacity of 1 g amal	Average (mayers)
		408.13			72.40		0.1397
A . . .	40.92	382.85	802.4	5.000	75.48	0.15701	0.1571
	40.92	382.85	800.8	4.999	75.48	0.15701	
	40.92	382.85	802.2	4.995	75.54	0.15716	
B	37.21	382.21	793.2	4.980	74.91	0.15578	0.1557
	37.21	382.21	792.6	4.982	74.83	0.15557	
C	32.69	387.87	800.4	4.980	75.6	0.15528	0.1553
	32.69	387.87	802.2	4.990	75.61	0.15531	
D.	27.69	400.295	815.6	4.990	76.87	0.15364	0.1534
	27.69	400.295	816.8	5.008	76.71	0.15324	
E	20.70	407.79	819.8	5.013	76.92	0.15094	0.1511
	20.70	407.79	817.6	4.992	77.03	0.15120	
F.. ..	15.40	420.14	831.0	4.996	78.23	0.14962	0.1496
	15.40	420.14	830.2	4.993	78.21	0.14957	
G	11.42	436.78	841.4	4.980	79.47	0.14676	0.1468
	11.42	436.78	841.8	4.980	79.51	0.14685	
H .	11.42	400.54	788.0	4.992	74.25	0.14700	0.1470
	11.42	400.54	787.6	4.988	74.27	0.14705	
I.	8.48	402.32	786.0	5.000	73.94	0.14558	0.1455
	8.48	402.32	785.4	5.002	73.85	0.14536	

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[1] Analyses of amalgams gave the following results A = 40.97, 40.88, 40.91, average 40.92% G = 11.42, 11.43, average 11.425% (calculated 11.42) L = 3.50, 3.49, average 3.495% (calculated 3.54) M = 34.91, 34.95, 34.84, 34.92, average 34.90%. U = 5.54, 5.53, average 5.535% (calculated 5.54) After each series the residual very dilute amalgams in the calorimeter were weighed, the weights being 405.7 and 401.9, respectively—reasonably near to the values calculated through the long chain of additions and subtractions

TABLE VII (*concluded*)

Designation of amalgam.	Thallium. %	Weight G	Time Seconds	Temp rise ° C	Total heat cap Mayers	Heat capacity of 1 g amal	Average (mayers).
J...	6 30	403 95	784 2	5 008	73 65	0 14428	0 1441
	6 30		783 6	5 013	73 52	0 14395	
K	4 69	405 18	780 0	5 005	73 30	0 14299	0 1431
	4 69		780 4	5 003	73 37	0 14316	
L	3 54	406 32	780 0	5 020	73 08	0 14203	0 1423
			780 0	5 003	73 33	0 14264	
			778 2	5 020	73 21	0 14234	
			779 8	5 020	73 06	0 14200	0.1423
			780 4	5 010	77 27	0 14250	
M	34 90	386 17	800 0	4 999	75 27	0 15511	0 1550
				5 010	75 09	0 15465	
				4 998	75 29	0 15516	
N	29 49	388 86	801 0	5 010	75 06	0 15350	0 1534
			795 4	4 990	74 97	0 15327	
P	24 88	391 40	799 2	5 008	75 06	0 15250	0.1523
			798 2	5 010	74 94	0 15220	
Q	18 36	394 40	790 0	4 990	74 47	0 14985	0 1499
			790 2	4 990	74 48	0 14987	
R	13 58	396 54	787 0	5 002	73 93	0 14768	0 1478
		396 54	787 0	5 002	74 00	0 14785	
S	10 07	398 32	780 0	4 995	73 45	0 14582	0 1458
			781 8	5 005	73 47	0 14587	
T	7 47	398 03	778 2	5 029	72 78	0 14391	0 1444
			780 0	5 017	73 13	0 14479	
			775 6	5 012	72 79	0 14393	
			776 8	5 005	73 00	0 14446	
			778 4	5 008	73 11	0 14474	
U	5 54[1]	399 80	773 2	5 005	72 06	0 14330	0 1433
			775 0	5 015	72 69	0 14337	
V	3 07	400 71	765 8	4 988	72 21	0 14185	0 1418
			770 0	5 018	72 17	0 14175	
W .	1 49	402 31	764 6	4 996	71 98	0 14071	0.1408
			764 8	4 995	72 02	0.14082	

These values are plotted in the accompanying graph (Fig. 6), which shows that only 2 of the 21 points are far distant from a smooth curve.

Schmitz[2] found the specific heat of solid metallic thallium (20–100°) to be 0 0324; hence the heat capacity of one g. is 0 1354 mayer—a value, as one would expect, not very different from that of lead. If no change of specific heat took place on amalgamation, a 40.9% amalgam should have the heat capacity of 0.1381 instead of the actual value 0.1571. The gain of 14% is unusually large, even taking account of the liquefaction of the thallium (for liquids usually, if not always, have a larger specific heat than the corresponding solids), and is especially interesting in view of the concomitant marked increase in volume. This adds another to the many cases in which these two changes go hand in hand—a category including the increase in volume and specific heat accompanying not only liquefaction in general, but also neutralization and other kindred phenomena involving the combination of ions. The most striking exception to the rule is the behavior of ice on melting.

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[1] The portion of this taken out in preparation for the next amalgam was analyzed.

[2] *Proc. Roy. Soc. London*, **72**, 177 (1903).

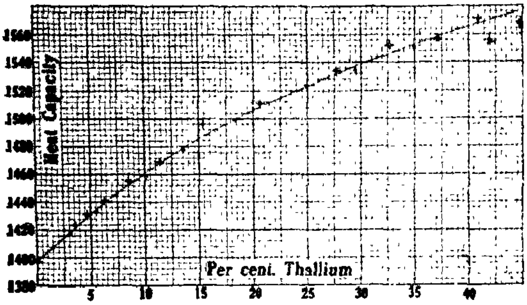

Fig. 6.—Heat capacities of thallium amalgams. Specific heat capacities (in joules/$t°$ = mayers) are plotted as ordinates, and percentage composition of amalgams as abscissas.

It is not without interest to refer the changes of heat capacity thus measured to a given constant quantity of thallium. This is most conveniently represented by determining a quantity which may be called the "solution heat capacity" of thallium, analogous to the "solution volume." The "solution heat capacity" is obtained by referring to the thallium all the change in heat capacity which occurs on amalgamation (although, of course, it is by no means certain that some of the change is not due to an effect upon mercury associated with thallium). This quantity gives another clue to the constitution of the solution, and is therefore of value.

The "solution heat capacity" may very simply be calculated by subtracting the heat capacity of the mercury $(100 - b)K_0/b$ of an amalgam having b % of thallium, from the heat capacity $100K/b$ of the amalgam. K_0 and K represent, of course, the heat capacities of a gram of mercury

Table VIII.

"Solution Heat Capacity" of Thallium

(Heat Capacity of 1 g of Mercury = 0.1397 mayer; of 1 g. Thallium = 0.1354.)

Composition of amalg. %.	Heat cap. per g. of amalg.	$\frac{100\,K}{b}$.	$\frac{100-b}{b}K_0$	"Solution heat cap." per 1 g thallium (mayer).
5	0.1431	2.862	2.654	0.208
10	0.1461	1.461	1.257	0.204
15	0.1486	0.990	0.792	0.198
20	0.1506	0.753	0.559	0.194
25	0.1523	0.609	0.419	0.190
30	0.1539	0.513	0.326	0.187
35	0.1552	0.443	0.259	0.184
40	0.1565	0.391	0.210	0.181

and of the amalgam, respectively. In this way the preceding table of solution heat capacities is easily calculated.

Evidently a gram of thallium produces less effect on the heat capacity in concentrated amalgams than in dilute ones, and we may safely infer that the circumstance or reaction which causes the greatly increased heat capacity occurs to a less extent in the concentrated amalgams than in the dilute ones. Presumably this effect is (at least in part) hydrargyration. In any case the increase is very striking being from 34 to 53% of the original heat capacity of the solid thallium (0.1354).

The change in the "solution heat capacity" is interesting in contrast to the approximate constancy of the solution volume, already tabulated (see p. 1745). Although these phenomena parallel one another as regards sign and order of magnitude, they cannot be due entirely to the same tendencies.

The Heat of Dilution of Thallium Amalgams.

In the preceding extended series of experiments on the heat capacity of the amalgams, the heat of dilution with pure mercury, in the calorimeter, was carefully observed at the times of preparation of the successive amalgams.

Mercury is so good a conductor of heat, and the total heat capacity in the calorimeter was so small, that it was necessary to make sure that the added mercury possessed really the same temperature as the calorimeter at the moment of introduction. In order to accomplish this result, the mercury was introduced from a water-jacketed pipet with a very fine point. The whole length of the delivery tube as well as the body of the pipet was surrounded by a current of water kept at exactly 20°, the starting point of the experiment (Fig. 7). A weighed amount of mercury having been introduced into the pipet (the weight having been found by the loss of weight of a weighing bottle containing mercury, from which it had been drawn by suction), and time having been allowed for it to attain the proper temperature, the mercury was allowed to run into the calorimeter, diluting the amalgam there. At all times during the transfers, as well as during the thermal measurement, the amalgam was protected from oxidation by carbon dioxide gas in the manner already described, and the last drop of mercury was ejected from the pipet by pressure of the same gas.

Since mercury is more dense than the amalgams, the pure liquid diffused thoroughly through the liquid mass

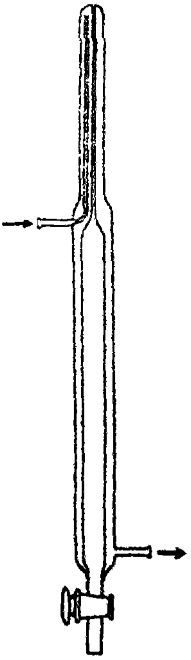

Fig. 7.—Water-jacketed pipet for delivering mercury isothermally.

almost immediately, and little stirring was needed, except in the case of the most dilute amalgams, where the densities of the two metallic liquids were nearly identical and somewhat more energetic stirring was needful

The following table records the results

TABLE IX

Heats of Dilution at 20°

Wt of amalgam in G.	Wt of mercury in G	% composition orig amalg	% comp'n resulting amalg	Rise of temp	Ht cap of system	Heat evolved Joules	$U_{20°}$ Heat ev per g at Tl
			First Series				
347.56	34.65	40.92	37.21	2.240°	74.87	168	241
340.78	47.09	37.21	32.69	2.780	75.60	209	337
339.05	61.25	32.69	27.69	3.070	76.79	236	433
304.91	102.88	27.69	20.70	4.023	76.97	309	747
312.60	107.54	20.70	15.40	2.712	78.22	211	666
323.73	113.05	15.40	11.42	1.798	79.49	143	585
298.75	103.58	11.42	8.48	1.010	73.90	74.6	446
300.35	103.60	8.48	6.30	0.630	73.59	46.4	372
301.42	103.72	6.30	4.69	0.347	73.33	25.5	273
302.52	103.81	4.69	3.55	0.175	73.19	12.8	181
			Second Series				
322.83	64.03	34.90	29.49	3.250	75.02	243	435
330.54	60.86	29.49	24.88	2.810	75.00	211	441
291.17	103.22	24.88	18.36	3.483	74.47	259	731
293.15	103.39	18.36	13.58	2.250	73.97	166	631
295.37	102.94	13.58	10.07	1.375	73.46	101	514
295.99	102.94	10.07	7.47	0.810	72.96	59	405
296.43	103.37	7.47	5.54	0.480	72.67	34.9	321
297.55	102.88	5.54	4.12	0.273	(72.43)	19.8	245
297.88	102.83	4.12	3.07	0.130	72.19	9.4	156
296.26	106.04	3.07	1.49	0.130	72.00	9.4	319

At the close of the seventh experiment of the second series the final result was tested twice by heating the system through 0.480° quantitatively, by means of the spiral electrically heated coil. The values obtained (34.7 and 34.6) agreed as well as could be expected with the result computed from the heat capacity—34.9. Similar tests were made after the eighth and tenth trials, affording sufficient confirmation of these results also, within the limit of error of experimentation. Therefore it is safe to conclude that the values given represent closely the heats of dilution of the several amalgams.

Since the electromotive force and its temperature coefficient were both measured more carefully at 30° than at 20°, it is therefore convenient for comparison to recalculate the heats of dilution to the higher temperature—an easy task, since the heat capacity change during the reaction is known. According to the equation of Kirchhoff, $\Delta U = -\Delta K.\Delta T$ (or, in this case, $\Delta U = -10\ \Delta K$), ΔK being the change in heat capacity involved in any given dilution where the total amount of thallium present was 204 g. (a gram-atom). Table VII contains the necessary data concerning the heat capacities, and the results of the calculation are contained in Table X following. The change in any one experiment was simply divided by the atom-fraction (n) present in order to give the value for the gram-atom k and w mean heat capacity per gram, and weight, respectively; subscripts 1, 2 and 3, signify the stronger and the weaker amalgams, and mercury, respectively. The values of k_1 and k_2 were read from the smooth curve of Fig. 6 given on page 1752, since the smooth curve really represents an average value corrected for accidental experimental error. The values for ΔU were then plotted and were found to lie approximately on the curve given by Fig. 8.

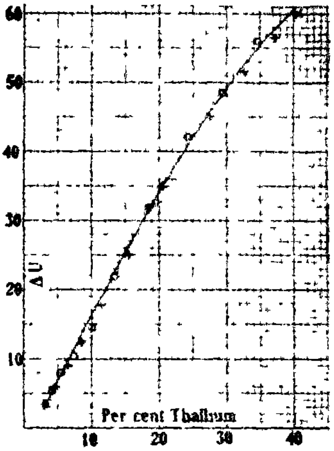

Fig. 8.—Change of dilution heat with 10° temperature change. ΔU (in this case the differences in kilojoules between the heats of dilution at 20° and 30°) are plotted as ordinates, and percentages of thallium are plotted as abscissas. Thus, for example, the curve shows that the dilution of a 40% to 20% amalgam (each containing 204 grams of thallium) evolves 26.5 kj less heat at 30° than at 20°.

For later reference the values for the heat of dilution of amalgam with mercury at 325° were desirable. Unfortunately, no data exist as to the heat capacity change over that large range of temperature, and it is hardly safe to conclude that the change will be the same as at room temperatures. Nevertheless, in default of other data, the values for 325° also were calculated, and are given in the last column. They make no pretensions to exactness, whereas the values at 30° may be considered as being almost as exact as those at 20°.

TABLE X

First Series

Comp. amalg	$k_1w_1 + k_3w_3$	k_2w_2	Δk	ΔU	$U_{20°}$	$U_{30°}$	$U_{325°}$
40.92 37.21	59.303	59.548	0.245	3.5	241	237	136
37.21 32.69	59.671	59.965	0.294	4.7	337	332	196
32.69 27.69	60.074	61.326	0.352	6.5	433	420	238
27.69 20.70	61.084	61.495	0.411	10.0	747	737	450
20.70 15.40	62.163	62.475	0.312	10.0	666	656	372

TABLE X (*continued*)

Comp. amalg.	*hm* + *hw*.	*hw*.	Δ*k*	Δ*U*	$U_{20°}$	$U_{30°}$	$U_{32.5°}$
15.40 11.42	63 932	64 119	0 177	7 0	584	577	368
11 42 8.48	58 326	58 418	0 092	5 5	446	440	281
8.48 6.30	58 084	58 138	0 044	4 0	[illegible]	368	252
6.30 4.69	57 864	57 894	0 030	3 0	273	270	198
4.69 3.55	57 732	57 780	0 048	7 ?	181	174?	(?)
			Second Series				
34.90 29.46	59 048	59 456	0 408	7 5	435	429	255
29.46 24.88	59 306	59 610	0 304	6 4	441	435	201
24.88 18.36	58 765	59 119	0 354	10 0	731	721	431
18 36 13.58	58 387	58 648	0 261	10 0	631	621	334
13 58 10 07	58 066	58 193	0 127	6 5	514	508	319
10 07 7 47	57 625	57 685	0 080	4 0	405	401	282
7.47 5 54	57 305	57 331	0 026	2 5	321	319	249
5 54 4 12	57 041	57 061	0 020	2 3	244	242	169
4 12 3.06	56 813	56 821	0 008	2 0	156	154	102
3 06 1 49	56 824	56 641	0 183	6	319	313	(?)

These results at 30° are plotted in the curve of Fig. 9 In plotting the two series together, the fifth experiment of the second series was made to lie exactly on the curve for the first set, for it is in this region that the results have the greatest accuracy and consistency. The origin was obtained by extrapolation. The graph gives at once the heat evolved by diluting an amount of amalgam containing one gram-atom from any given percentage to any other percentage, at 30.0°.

The Heat of Solution of Thallium in Mercury and in Thallium Amalgams.

A phenomenon closely related to that just treated, and of value in the verification of its significance, is the heat of solution of metallic thallium in liquid thallium amalgams. The explanation of the connection between the two diverse phenomena will be deferred until the second has been considered in detail.

Thallium dissolves easily and promptly in mercury, the first portion evolving considerable heat, and the later portion absorbing much more. The problem was to determine the magnitude of these thermal quantities.

The magnitude of the cooling effect may be determined simply by preventing the amalgam from being lowered in temperature, with the help of the quantitative heating coil described in the heat capacity experiments, noting the potential and quantity of the current. Through this isothermal method, a knowledge of the heat capacity is unnecessary. The amalgam is always at the temperature of the surroundings, and all cooling corrections are eliminated. The experiment may therefore extend over a considerable period of time, and equilibrium may be attained without rapid stirring. The method appears to be an extremely satisfactory one, but it can be used only for endothermic reactions. The apparatus consisted simply of a Dewar bottle (containing the amalgam, a heating coil, and a Beckmann thermometer) attached to the end of a large glass tube and submerged deep in a thermostat. The voltage across the heating coil was measured with a potentiometer, and a silver coulometer gave the quantity of electricity passing.

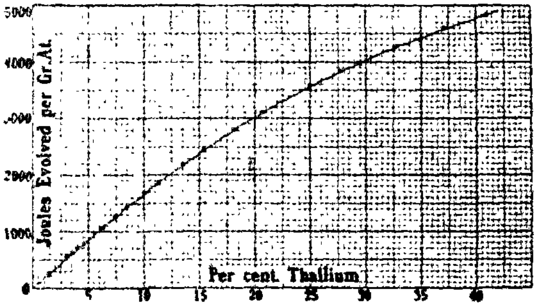

Fig. 9.—Heat of dilution of thallium amalgams at 30°. Ordinates indicate joules evolved on diluting a mass of amalgam containing one gram-atom of thallium. Abscissas indicate percentage composition.

The procedure, as evolved in the course of a few preliminary experiments, was as follows: A suitable quantity of mercury was put into the calorimeter, and when its temperature was the same as that of the thermostat (30°) it received successive weighed amounts of thallium. Occasional stirring with a small glass rod caused uniform mixing. Previously the oxide had been removed from the thallium by treatment with a little standard acid, due correction being applied to the weight taken. The thallium pieces had also been placed in a small bottle immersed in the thermostat, so that the whole system would be at the same temperature. Oxidation was nearly, but not completely, eliminated by a layer of purified kerosene in the calorimeter.

The heating of the coulometer with the passage of the current caused a rapid decrease in its resistance, and consequently a tendency to increase the fall of potential across the heating coil. Although this was corrected as rapidly as possible by the arrangement provided for that purpose, the compensation was not always exact, and the results must be regarded merely as preliminary. The arrangement described under the heat capacity determinations, including the stop watch, was far more satisfactory, and would have served the purpose better. It is intended not only to verify the present preliminary results by repeating the experiments with larger amounts of material, but also to extend the method to many other cases, both of amalgams and aqueous solutions producing endothermic reactions.

As already said, the first portions of thallium on dissolving in mercury caused a *rise* of temperature. This could not be measured accurately, since the heat capacity of the Dewar vessel was unknown. The procedure, therefore, until the concentration had attained 8.76%, was not thermally quantitative, but was interesting in showing that a considerable amount of heat was at first evolved. Every addition after the percentage just named caused a cooling effect and this could be accurately measured. These results are accordingly included in the table given below. After the amalgam reached the concentration of 38%, the liquid became so nearly saturated that the thallium dissolved very slowly and the results were of little value. Therefore they are not included in the table.

TABLE XI

The Heat of Solution of Thallium in Mercury

(240.546 g. of Mercury in the Calorimeter.)

Expt	Tl present	Tl added	% Tl in resulting amalgam	Per cent of a g. at. of Tl added, 100n	Per cent of a g. atom present	Heat involved in process, Δw
1...	0.0000	15.9457	6.22	7.82	7.82	(150)[1]
2.	15.9457	7.1497	8.76	3.50	11.32	(50)[1]
3.	23.0954	6.2125	10.86	3.05	14.37	1.0
4...	29.3079	13.9567	15.24	6.84	21.21	52.8
5....	43.2646	14.6875	19.42	7.20	28.41	116.2
6.....	57.9521	16.5595	23.65	8.12	36.53	−188.5
7......	74.5116	16.4778	27.45	8.08	44.60	−219.0
8[2]....	64.6504	11.6705	30.87	5.72	37.41	−173.7
9......	76.3209	13.4104	34.43	6.57	43.99	−217.6
10......	89.7313	15.4190	38.09	7.56	51.54	−277.3

In tabulating these results, it was remembered that the concentration of the thallium in the amalgam increases as the thallium dissolves. Thus in any single experiment the first portion dissolved corresponds to the addition of thallium to an amalgam of the lower (original) concentration, while the last portion corresponds to the addition of thallium to an amalgam of the higher (final) concentration. The heat evolved therefore corresponds approximately to the addition of thallium to an amalgam of the average concentration. For example, the heat evolved (—1614 joules) during the increase of concentration from 15.24 to 19.42% must correspond closely to the addition of a gram-atom of thallium to an amalgam of the average concentration 17.33% (as given in the middle column of the following table). This calculation assumes, of course, that the curve is practically a straight line between the two concentrations—an assumption which would be strictly permissible only for very small additions of thallium. Nevertheless, the small error thus introduced is clearly less than the probable experimental error. The middle column, and the method of arranging the figures, below, are obvious outcomes of these considerations. The heat evolved in each case is reduced to the gram-atom standard by dividing the heat evolved (nU) on the solution of the thallium in each case by the fraction (n) of a gram-atom added.

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[1] In giving these approximate values an approximate value was assumed for the heat capacity of the Dewar flask. Account was taken also of the extrapolation of the more certain part of the curve, and of the requirement of the Helmholtz equation.

[2] 99.9708 g. of the amalgam was removed at this point. 170.914 g. Hg now present.

TABLE XII

Heat of Solution a Gram Atom of Thallium in Amalgams

% Tl in successive amalgams	Average % Tl during each addition	nU/n Heat evolved in dissolving one gram atom of Tl in amalgam
8.76		
	9.81	— 32
10.86		
	13.05	— 773
15.24		
	17.33	—1614
19.42		
	21.53	—2321
23.65		
	25.55	— 2711
27.45		
	29.16	—3036
30.87		
	32.65	3310
34.43		
	36.26	— 3670
38.09		

The average values from the middle column are plotted in relation to the heat values from the last column, in the accompanying graph (Fig. 10). The points do not lie on a perfectly smooth curve, but in drawing the curve the effort of compromise was made to distribute the errors by making the divergent points about equidistant from a reasonable locus. The error of the most divergent point is about 7% of the value; none of the other errors exceeds 5%. Although the accuracy leaves much to be desired the present to illustrate the principles involved, and is therefore much better than nothing.

These values may be looked upon as containing separate factors; first, the heat absorbed when the solid melts or dissolves to form a saturated solution, and secondly, the heat evolved when the saturated solution becomes diluted to the resulting amalgam. When the dilution is great, the positive effects overbalance the negative and the net result is the evolution of heat, as seen at concentrations below 9.6%.

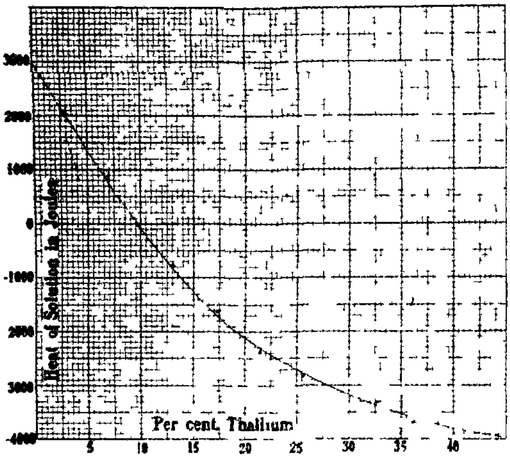

Fig. 10.—Heat of solution of a gram atom of thallium in thallium amalgams. Abscissas indicate percentage composition of amalgams.

Since thallium increases greatly in heat capacity on amalgamation it is evident that the thermal values given in the preceding table (XII) are subject to considerable change with temperature. Because the specific heats of the several amalgams are known, as well as the specific heat of thallium, this change is easily calculated by Kirchhoff's equation, in a manner analogous to that employed in the heats of dilution of thallium amalgam. For example, 100 g. of a 28% amalgam, on the addition of 4 g. of thallium produces 104 g. of a 30.77% amalgam. The heat capacity of the weaker amalgam and of the thallium separately aggregates 15.87 mayers; that of the concentrated product, 16.03 mayers. The gain in heat capacity corresponding to 4 g. of thallium is therefore 0.16 mayer. This, divided by n, the atom fraction, gives 8.16, which is $\Delta K = -\frac{\Delta U}{\Delta T}$. Three such results, all calculated from the smooth heat capacity curve (Fig. 6) are given below. The composition of the concentrated amalgam is represented by a; that of the dilute amalgam by b; K_4 signifies the heat capacity of a gram of thallium.

At first sight this table seems to be simply a repetition of that recording the solution heat capacity of one gram of thallium, with the heat capacity of the original thallium itself not included, and indeed it would be easy to show that the two tables are entirely parallel, representing, as they do, very similar phenomena. But they are not exactly alike, the earlier one records the gain in heat capacity when thallium is added to mercury, whereas the table just given records the gain in heat capacity when thallium is added to a thallium amalgam.

TABLE XIII

b	a	Mean.	Wt Tl added	$K_{2}w_{2} - K_{1}w_{1}$	$K_{1}w_{1}$	$\Delta K = \frac{n\Delta U}{\Delta T}$	$\frac{\Delta U}{\Delta T}$
40 00	42 31	41 16	4	16 19	16 34	0 15	7 6
28 00	30 77	29 39	4	15 87	16 03	0.16	8 2
18 00	21 15	19 58	4	15 52	15 70	0 18	9 2
10 00	13 46	11 73	4	15 15	15 37	0 22	11 2
5 00	8 65	6 83	4	14 85	15 11	0 26	13 3

The present table shows even more clearly than the other that the increase in heat capacity on adding thallium decreases as the concentration increases. The outcome is interesting in showing the large temperature coefficient, varying from 7 6 to 13 3 joules per degree, shown by the amalgamation of thallium, as well as the very considerable difference in heat capacity which must be suffered when thallium is transferred from a more concentrated to a more dilute amalgam, as during the operation of the amalgam cells under consideration. This last quantity is shown by the difference between the successive figures in the last column of the preceding table. The exhibition of this difference represents the main use of the table, and will be treated in detail later. Since the main comparison involved in the present work is made at 30°, the other possibilities of the table need not be discussed.

The Calculation of the Total Energy Change Involved in the Cell.

The total energy change (U of the equation of Helmholtz) involved in the cell has already been calculated from the temperature coefficient of the electromotive force. U is also to be found when the values given in the last column of Table XII, and plotted in Fig. 10, since the difference between any two of these values must give the heat of transfer of a gram atom of thallium from one to the other of the corresponding amalgams (*i. e.*, $U = \frac{n_1U_1}{n_1} - \frac{n_2U_2}{n_2}$).

Besides these two methods, yet a third method of calculating this quantity U exists, depending upon the heat of dilution of thallium amalgams with pure mercury. Formerly the assumption has often been made that the heat evolved in diluting an amount of amalgam containing a gram equivalent of dissolved metal is identical with the heat of transfer of the aforesaid gram equivalent between the initial and final amalgams.[1] This is far from being the case; indeed, the former is only about half of the latter. The presence of some sort of inconsistency here was recognized in the earlier Harvard papers, and therefore the heats of dilution were rejected, without, however, attempting to discover its reason. In the sequel, the situation is fully explained.

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[1] See for example Cady, *J. phys. Chem.*, 2, 562 (1898). Cady's actual measurements of the heat of dilution of sodium amalgams must have [illegible] values

When mercury is added to a liquid thallium amalgam, two processes occur simultaneously; first, some of the thallium is taken from the mercury originally present; second, this thallium is (at the same instant) dissolved in the new pure mercury. Only the first of these processes is parallel with anything that happens in the cell under consideration, since the cell has nothing to do with pure mercury.

Clearly, in order to calculate the heat-effect in the cell from the heat of dilution, the second of these two simultaneous processes must be eliminated. This may easily be done by causing two different concentrated amalgams to be diluted separately to the same final condition. Then, by multiplying each of the two heat values, thus found, by an appropriate factor corresponding to the amount of thallium transferred (so as to transform each into a value corresponding to the *transfer* of a *gram-atom* of thallium), two results are obtained which involve the formation of exactly the same amount of dilute amalgam made from newly added pure mercury. By subtracting these two values, the second of the two simultaneous processes is thus entirely eliminated. The difference between them becomes simply equal to the heat of transfer of a gram-atom of thallium between amalgams having compositions represented by the *average* compositions over the two respective ranges of dilution.

Since the problem is somewhat unusual, it may profitably be exemplified by a specific case.

In any given dilution let a equal the per cent. of thallium in the initial concentrated amalgam, b equal the per cent. of thallium in the resulting dilute amalgam, and x equal the amount of mercury added. Then $\frac{a}{100 + x} = \frac{b}{100}$, and $x = \frac{100\,a}{b} - 100$. Further, $\frac{(100 - a) + x}{(100 - a)} = 1 + \frac{100(a - b)}{(100 - a)b} = c$, (in which $c : 1$ is the ration of the total amount of mercury to that originally present); and the amount of thallium *transferred* must be the fraction $\frac{c - 1}{c}$ or $\left(\frac{100(a - b)}{a(100 - b)}\right)$ of a gram-atom, if the heat of dilution is calculated for the *total* amount of a gram-atom present. Hence this heat of dilution divided by the atom-fraction $\frac{c - 1}{c}$ gives the amount of heat involved in the *transference* of a gram-atom of thallium from the more concentrated amalgam into mercury, under such conditions that the product possesses the concentration of the more dilute carried out for the dilution of two concentrated amalgams to the same final concentration, and the heat-effect for each transfer is calculated for a gram-atom. In practise it is not necessary to calculate the values of x and c, since the fraction $\frac{c-1}{c}$ may be expressed entirely in terms of a and b, as indicated above. As already stated, subtraction of the one result for the gram-atom from the other gives the heat of transfer from a solution corresponding to the average concentration over the first range to that of a solution having the average concentration over the second range. The detailed steps of the calculation for the two ranges, 40% to 30% and 35% to 30% follow, as an example of the method of calculation.

Table XIV

Composition %	G Hg per 100 g amalgam	x = g mercury added	Dilution factor	Observed heat of dilution	Heat of dil'n per g-atom of thallium
a = 40.0	60.0	33.33	1.5555	740	2072
b = 30.0	70.0				
a' = 35.0	65.0	16.67	1.2565	400	1959
b' = 30.0	70.0				
				U =	113

Algebraically, if q and r represent, respectively, the heat of removal of a gram-atom of thallium from the two concentrated amalgams, and m the heat of adding this thallium to mercury (the same in each case), then $q + m = 2072$ and $r + m = 1959$; subtracting, $q - r = U = 113$. Thus although we do not know, and have no means of knowing any one of the quantities q, r, and m individually, we are able to determine $q - r$ definitely. The result $q - r = U = 113$ joules represents the heat evolved when a gram-atom of thallium is transferred from an average concentration of 35% to an average concentration of 32.5%, the respective means (that is $^1/_2(a + b)$, and $^1/_2(a' + b')$) of the two ranges involved.

From the succession of pairs of values obtained in this way, step by step, the curve labelled SD in Fig. 11 was built up.

It is of course true that the curve SD, Fig. 11, thus produced does not exactly represent the true values, since it is rather made up of a series of straight lines than a strictly continuous curve. It is, however, very near the real curve, which would lie slightly above it (nearer to the curve H), and is probably accurate within the limit of error of the experiment. Greater accuracy could be attained by taking shorter intervals and more points, but this extra trouble is not warranted by the precision of the present experimental work.

Since this curve cannot be continued to infinite dilution, its origin must be found by extrapolation, but this is a matter of minor importance

It should, of course, coincide with the values for U given by the Helmholtz equation (curve H, Fig. 11), and for great dilutions the latter is doubtless more accurate than the former can be. Therefore, instead of attempting an extrapolation, the curve D was started on the curve giving the values for the Helmholtz equation at about 8% amalgam.

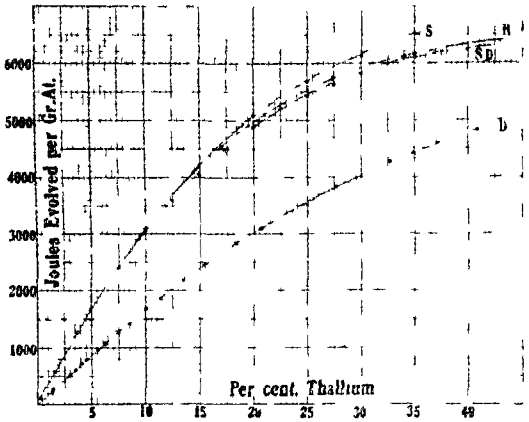

Fig. 11.—Heat of transfer of a gram atom of thallium from one amalgam to another of different concentration. Curve S, as calculated from the heat of solution of thallium; Curve D, as calculated from the heat of dilution of thallium amalgam; Curve H, as calculated from the Helmholtz equation. Curve D gives the heat of dilution.

In order to show the degree of consistency of the 3 methods of calculating U, namely, from the heat of solution of thallium on the one hand, from the heat of dilution of thallium amalgam on the other hand, and from the Helmholtz equation (see page 1761), the following table is given, exhibiting values taken (as regards the first two methods) from curves plotted on a much larger scale than the appended diagram.

TABLE XV.

Heat Effect in Cell (U).

(In Joules per Gr. Atom of Tl Transferred.)

I Conc. in cell.	II Found from heat of solution of Tl.	III Found from heat of dilution of amalgams.	IV Calculated from Helmholtz equation.
0.3315–1.704			470
0.1704–3.788			696
3.788–4.935			370
			—
4.930–10.02	1440	1420	1449
10.02–17.05	1530	1400	1445
17.05–21.02	625	570	568
20.97–27.36	705	647	631
27.36–34.03	460	400	385
34.03–42.86		240	261
		—	—
Sum, 4.93–42.86		4677	4739

The values in Col. II have a large probable error, and are valuable only as a general confirmation of the others. The values in Col. III are much more trustworthy, and those in Col. IV are

Since the agreement of Cols III and IV is within the limit of the series of experimental errors of the two columns, evidently the Helmholtz equation is confirmed in its application to these amalgam cells, taking account of the fact that the thermal effect to be considered is the transfer of thallium from a concentrated amalgam of definite concentration to an equally definite more dilute amalgam.

The Freezing Points of the Amalgams.

One other phenomenon which throws light upon the behavior of thallium, and therefore upon the nature of the solutions in mercury, deserves consideration, namely, their irregular freezing-point curve. There can be no doubt that these freezing points, through eutectic and dystectic breaks in the curve, indicate the existence of a solid compound. The work of Kurnakow and Puschin[1] seems to show a compound of the composition $TlHg_2$, but our experience (communicated below) indicates rather the formula Tl_2Hg_5. Some years after our determinations were made, but of course entirely independently, since our results had not been published, Roos[2] published results similar to ours.

TABLE XVI

% Tl by weight	Atomic %	Temp of freezing °C
1913. First Series (Small Quantities.)		
42.8	42.3	+1.6
38.8	38.3	5.3
34.0	33.5	12.0
31.7	31.3	13.9
29.1	28.7	14.9
26.4	26.0	14.3
24.2	23.8	12.3
19.5	19.2	3.0
1913. Second Series (Small Quantities.)		
36.5	36.0	9.2
34.4	33.9	11.7
31.5	31.1	14.1
29.0	28.6	14.8
25.4	25.0	13.2
23.8	23.4	11.5
20.0	19.7	4.0
1914. Third Series (Beckmann Freezing-Point Apparatus.)		
40.90	40.47	+0.9[3]
38.83	38.37	5.9[3]
37.19	36.71	9.5[3]
32.63	32.31	12.8[3]
27.60	27.24	14.3
20.63	20.31	5.7
18.27	17.97	−0.9
16.92	16.65	−6.5

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[1] Kurnakow and Puschin, *Z. anorg. Chem.*, **30**, 86 (1902).

[2] Roos, *Ibid.*, **94**, 358 (1916); *C. A.*, **10**, 1479 (1916).

[3] In these experim

In 1913 crude experiments were performed with concentrated amalgams from the electromotive force experiments. A small glass bulb containing the amalgam was slipped over the thermometer bulb and tightly held with a rubber ring. The thermometer was read when the amalgam started to freeze upon being plunged into cold water. After complete solidification the bulb and thermometer were removed from the cold bath and the instrument was read again as the last portion of the solid amalgam was disappearing. With each amalgam several trials and successive readings were made. Successive portions of mercury were added and the process repeated again and again.

A year later further experiments were made, using a Beckmann freezing-point apparatus with large quantities of amalgams from the calorimetric determinations. These confirmation determinations are much more accurate than the preceding.

In Fig. 12 these values are represented by small circles. The curve attains a maximum in the neighborhood of 28.5 atomic % of thallium. This dystectic point shows then that a compound of thallium and mercury is formed corresponding to the formula Tl_2Hg_5. Convincing proof of such a compound lies in the fact that amalgams of approximately this composition gave a sharply defined melting point and remained stationary at this temperature (14.9°) during the whole time of freezing. All other amalgams (including those (corresponding to $TlHg_2$) or 33.3 atomic %) gave ill-defined freezing points, which changed during solidification. For instance, the 36.71% amalgam started to freeze at 9.5°, but was not completely solid even at 5.0°. Solid amalgams of approximately 28.5% consisted of perfect crystals, while all the other amalgams gave ill-defined crystals. This is to be taken as further evidence of the existence of a compound Tl_2Hg_5.

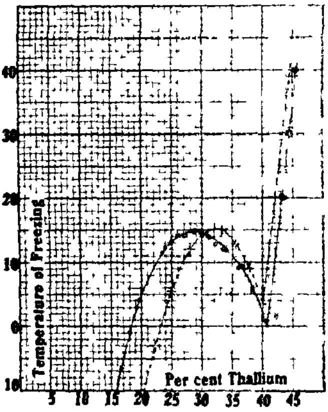

Fig. 12.—Freezing points of thallium amalgams. Dotted curve indicates results of Kurnakow and Puschin. Abscissas indicate atomic %. (In all other diagrams abscissas indicate per cent by weight.)

The double circles represent freezing points as determined from the electromotive force measurements, being the breaks in the curve already illustrated in Fig. 3. Freezing points at 40°, 30° and 20° were found, respectively, to be at 45.8, 44.5, and 43.3%. This line extrapolated crosses the curve of the freezing point of the weaker amalgam at about 40.8%, the temperature being about 0.5°, and thus giving a wholly consistent picture.

The dotted line in Fig. 12 indicates the freezing points of thallium amalgams as determined by Kurnakow and Puschin.[1] This curve shows a maximum of 15.0° at $33\frac{1}{3}\%$ instead of at 28.5%, and seemed to its authors to indicate the existence of the compound $TlHg_2$. The eutectic point at 40% is likewise not in agreement with ours. Experimental details are not given and the cause of the serious discrepancy cannot be determined. Certainly the purity of the materials in the present research is beyond question, and the fact that our electromotive-force measurements (Fig. 3) gives a perfectly regular curve shows that the concentrations must be correctly known. Cohen and Inouye[2] have repeated Puschin's work on the zinc amalgams and found it considerably in error, and they suggest that his work on other metals may be in need of revision. The erroneous freezing-point curve for thallium amalgams has been copied in a text-book[3] as an example of the indication of a compound ($TlHg_2$) by a dystectic point.

The conclusion that the formula of the solid compound is really Tl_2Hg_5 is of interest as regards the constitution of the liquid amalgams, because it shows that thallium has a tendency to form diatomic molecules. If diatomic molecules thus exist in the solid state, it is not unreasonable to believe that the same tendency may exist in solutions.

Conclusion.

Thus a great variety of data concerning the nature of thallium amalgams has been provided, and some of the essential thermodynamic relations between these phenomena have been pointed out. The more detailed hypothetical analysis of these varied data is capable of furnishing much light on the nature of amalgams as well as on the nature of solutions in general; but this is a large subject, involving the discussion of bicomponent systems in its widest bearings, and is reserved for a later paper, now almost ready for publication.

We are much indebted to the Carnegie Institution of Washington for financial support in this investigation, and to Dr. W. C. Schumb for assistance in the manifold and time-consuming calculations involved.

Summary.

In this paper the following contributions to the experimental study of thallium amalgams have been made:

1. The electromotive forces between amalgams ranging from 0.33% to saturation (over 40%) have been measured within a few microvolts, at 20°, 30°, and 40°. These potentials are far greater than those demanded by the simple concentration law.

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[1] Kurnakow and Puschin, *Z. anorg. Chem.*, **30**, 86 (1902).

[2] Cohen and Inouye, *Z. phys. Chem.*, **71**, 627 (1910).

[3] Findlay, "The Phase Rule," p. 225, Longmanns Green and Co., New York

2. The temperature coefficients of the electromotive forces of these amalgams have been computed from these results. These temperature coefficients are less than the requirement of the gas law, and vary as the concentration increases.

3. The densities of the liquid amalgams and the solution volume of thallium in mercury have been determined over the whole range. The solution volume is remarkably constant, varying only from 17.47 to 17.51, but is somewhat in excess of the specific volume of thallium, 17.21. Thus thallium expands on amalgamation.

4. The coefficients of expansion of the various amalgams were computed from these results. They diminish with increasing concentration.

5. The heat capacities of the amalgams were determined by a somewhat new method over the whole range. They were found to be distinctly in excess of the sum of the heat capacities of the thallium and mercury taken separately; that is, the "solution heat capacity" of one gram of dissolved thallium is greater than the heat capacity of one gram of solid thallium. This excess is greater in dilute than in concentrated amalgams.

6. The heats of dilution of thallium amalgams with mercury at 20° were determined over the whole range of concentrations. With the help of the heat-capacity values these results were corrected to 30° (and approximately to 325°).

7. The heats of solution of thallium in mercury and in thallium amalgams of increasing concentration were measured.

8. Although the heat of dilution of thallium amalgam is a very different effect from the transfer of thallium from one amalgam to another, one of these effects can be computed from the other. The necessary steps are indicated.

9. It is shown that, within the limit of error of the experiment, the heat effects in the cells of which the electromotive forces were measured may be computed from either the heat of dilution of the amalgams, or the heat of solution of thallium in the amalgams, or the temperature coefficient of the electromotive force—each of these 3 methods giving essentially identical results within the limit of error of the experiment.

10. The freezing points of amalgams from 16 to 45 atomic % were repeatedly determined, and were found to give a curve indicating conclusively the existence of the solid compound Tl_2Hg_5.

11. The single potential of pure electrolytic thallium was found to be about 2.5 m. v. more negative than that of saturated thallium amalgam at room temperatures.

CAMBRIDGE, MASS.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CORNELL UNIVERSITY.]

BEHAVIOR OF THE HYDRONITROGENS AND THEIR DERIVATIVES IN LIQUID AMMONIA. VI. ELECTROLYTIC NITRIDATION OF VARIOUS ANODES IN A SOLUTION OF AMMONIUM TRINITRIDE.[1]

BY A. W. BROWNE, M. E. HOLMES AND J. S. KING

Received August 11, 1919.

Attention has already been called by investigators in this laboratory to the similarity that exists between the peroxides and the pernitrides, and between the processes of oxidation and nitridation.[2] Turrentine[3] has adduced evidence in support of the view that hydronitric acid is a nitridizing agent, analogous in both structure and behavior to nitric acid. Welsh[4] has shown that sodium hydrazide probably undergoes ammonolysis in liquid ammonia, with formation of sodium amide, ammonia, and nitrogen, just as sodium peroxide undergoes hydrolysis in water, with formation of sodium hydroxide, water, and oxygen.

In the fifth article of the current series were recorded the results of an investigation upon the behavior of a solution of ammonium trinitride in liquid ammonia when electrolyzed between platinum or graphite electrodes. From this work it may be concluded that under suitable conditions either nascent nitrine, N_3, which at once breaks up into molecular nitrogen, or nascent nitrogen, N, can be liberated at the anode. It has been the purpose of the present investigation to ascertain whether or not nitridation of certain metallic anodes will take place, under similar conditions, with formation of the corresponding metallic nitrides or pernitrides. Anodes of copper, silver, cadmium, aluminum, lead, antimony, iron, and nickel were employed in the experiments to be described.

Apparatus and General Procedure.—The H-tube described and figured in Article V[5] of this series was used throughout the greater part of the work. This cell was provided with two electrode tubes, as before, for the collection of gases liberated during electrolysis. Through the anode tube, however, instead of the slender wire attached directly to the platinum electrode, was fused a short piece of heavy platinum wire, terminating on the inside of the tube in a flattened hook into which the bent-over end of an electrode could readily be drawn so as to give a satisfactory contact. The cathode used with this apparatus consisted of a piece of smooth platinum foil 2 cm. long and 0.5 cm. wide.

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[1] For the earlier articles of this series see THIS JOURNAL, 33, 1728–34, 1734–42, 1742–52 (1911); 35, 649–58, 672–81 (1913).

[2] See Browne and Welsh, *Ibid*., 33, 1728 (1911); Goldberg, *Ibid*., 34, 886 (1912).

[3] *Ibid*., 34, 385–7 (1912). See also Turrentine and Moore, *Ibid*., 34, 375–382, 382–384 (1912).

[4] *Ibid*., 37, 497–508 (1915).

[5] [illegible]

At the beginning of an experiment the carefully cleaned, dried, and weighed anode was suspended in the tube. The electrode tubes were then set in position in the cell, into which had been placed 1.000 g. of pure ammonium trinitride. After the air had been displaced with pure, dry ammonia gas, 36 cc. of liquid ammonia was condensed in the apparatus with the aid of solid carbon dioxide and alcohol, and the solution was thoroughly stirred. The gases liberated during electrolysis were collected, transferred, and analyzed in the usual way. Immediately after the completion of the electrolysis, which was conducted at a temperature of about —67°, the anode was quickly detached, was cleansed from adhering deposits, in case any were formed, and was washed, dried, and weighed in the usual manner. The cell was finally allowed to warm up to room temperature, and the residual solid obtained by evaporation of the liquid ammonia was subjected to further tests as outlined below.

Details of the Experiments.—The principal numerical details of the individual experiments are recorded in the table. Additional results are appended in the paragraphs that follow.

TABLE I

No. of expt.	Anode used	Anode loss G	Coulometer cath gain G	Electrochem effic corrosion Per cent	Nitrogen evolved at anode (corrected) Cc	Nitrogen evolved at anode (corrected) G	Hydrogen evolved at cathode (corrected) Cc	Hydrogen evolved at cathode (corrected) G	Calc wt hydrogen G	Av current Milliamps
1...	Copper	0.0925	0.0645	143.4	none					100
2....	Copper	0.0489	0.0347	140.9	none					.
3....	Copper	0.0990	0.0688	143.9	none		23.44	0.00211	0.00218	110
4.	Copper	0.1274	0.0916	139.1	none		22.50	0.00202	0.00290	75
5....	Silver	0.2664	0.0775	101.3	none		30.30	0.00272	0.00246	100
6...	Silver	0.1549	0.0452	101.0	none					150
7..	Cadmium	0.1369	0.0768	100.8	none		25.44	0.00229	0.00244	100
8....	Cadmium	0.1451	0.0810	101.3	none					70
9.	Aluminum	0.0274	0.1143	84.3	3.80	0.00502	39.70	0.00357	0.00363	45
10....	Aluminum	0.0288	0.1168	86.8	4.73	0.00626	34.28	0.00308	0.00370	35
11....	Aluminum	0.1712	0.7846	76.8						390
12...	Aluminum	0.4378	1.9126	80.5						400
13...	Aluminum	0.4339	1.9301	79.1						1000
14....	Aluminum	0.5082	2.4902	71.8						1000
15....	Lead	0.3068	0.0922	102.1	none		29.49	0.00265	0.00292	110
16....	Lead	0.1661	0.0490	104.1	none					100
17...	Antimony	0.1264	0.0962	104.2	none		34.59	0.00311	0.00305	180
18...	Antimony	0.1882	0.1457	102.5	none		51.53	0.00463	0.00462	135
19....	Iron	0.0332	0.1340	42.3	15.60	0.0206	45.33	0.00408	0.00425	80
20...	Iron	0.0364	0.1309	47.5	16.87	0.0223	37.95	0.00341	0.00415	50
21....	Nickel	0.0547	0.1073	55.2	9.48	0.0125	34.67	0.00312	0.00340	95
22....	Nickel	0.0653	0.1078	65.6	5.44	0.0072	34.19	0.00307	0.00342	73

Expt. 1.—The anode consisted of a strip of sheet copper 2 cm. long and 0.5 cm. wide. Before the circuit was closed the cell was allowed to

suffer chemical corrosion when allowed to rest in contact with the electrolyte. No such corrosion was found to take place. As soon as the circuit was closed, however, a distinct blue coloration was observed in the neighborhood of the anode, and before long a layer of deep blue solution had accumulated in the bottom of the anode compartment. The anode was partly coated with a black deposit.

Expt. 2.—The deep blue solution remaining after the completion of the electrolysis, which was carried out under conditions similar to those prevailing in Expt. 1, was allowed to warm up until the liquid ammonia had completely vaporized. The solid residue was treated with water, and the light green precipitate resulting from hydrolysis of the copper salt was removed by filtration. No indication of the presence of hydrazine, the formation of which during the electrolysis had been regarded as at least remotely possible, was obtained when the filtrate was treated with Fehling's solution. The light green precipitate was thoroughly washed with water to remove the ammonium trinitride, and was then treated with a solution of ferric chloride. The deep red coloration indicated the presence of the N_3 group in the solid, which was undoubtedly a basic copper trinitride.

Expt. 3.—A copper anode having a surface (on one side) of 3.25 sq. cm. was used in this experiment. After an exposure of 3 hours to the action of the electrolyte before the current was passed through the cell, the anode seemed to have undergone a very slight chemical corrosion, as indicated by the appearance of a faint blue coloration in the anode compartment.

Expt. 4.—The same electrolyte was used in this as in the preceding experiment. The anode was removed and weighed, and then returned to the cell with suitable precautions to avoid the introduction of moisture. After completion of the electrolysis, which was continued for about an hour, the cell was allowed to warm up to room temperature. The solid residue, which contained ammonium trinitride and the copper salt formed as the corrosion product, was treated with water, which readily dissolved the former, but only slightly dissolved the latter constituent. The solution was decanted from the dark green crystals, which were then dried on filter paper without further washing, and were preserved for subsequent examination. Treatment with water was found to result in immediate hydrolysis, with formation of the light green basic trinitride[1] to which reference was made in connection with Expt. 3. On the other hand, treatment of the basic trinitride with ammonium trinitride caused a reversal of the hydrolytic action, with formation of the dark green crystalline product, which ultimately went into solution completely. For example, 0.06 g. of the dark green salt was treated with 3.7 cc. of water. The light green precipitate thus formed was changed back by 0.3 g. of solid ammonium trinitride. When treated under similar conditions with ammonium chloride the precipitate did not redissolve. The presence of bivalent copper, of N_3, and of ammonia, in samples of the original dark green crystals was established by the usual tests. The crystals were insoluble in water, but were soluble in dilute acids. They were found to explode with a loud report when heated. The amount of material obtainable was not sufficient to permit more accurate determination of its decomposition. From qualitative tests, however, it would seem to be either an ammonated cupric trinitride,[1] such as $CuN_6.2NH_3$, or possibly a cupric ammonium trinitride.

It will be noted from the data given in Column 5 of the table that in Expts. 1 to 4 the anode corrosion efficiency is considerably above 100%, as calculated on the basis of the ratio $Cu . 2N_3$. In the absence of appreciable chemical corrosion this indicates that formation of cuprous trinitride, CuN_3, must have taken pace to some extent.[2]

Expt. 5.—The silver anode used in this and in the following experiment was 0.75 cm. wide, and was immersed to a depth of 8 cm. The electrolysis was continued for 30 minutes. As was usual in these experiments, the corrosion took place chiefly at the lower end of the electrode owing to the special construction of the cell, which was designed so as to permit the collection of the gases liberated at the electrodes. After completion of the electrolysis the anode was removed and reweighed, and was again inserted in the cell, in preparation for the next experiment No evolution of gas, change of color, or formation of a solid deposit occurred at the anode. A heavy deposit of metallic silver gradually accumulated upon the cathode

Expt. 6.—The electrolysis was allowed to proceed for 30 minutes under conditions the same as those prevailing in the preceding experiment. The deposit of metallic silver on the cathode extended outside of the electrode tube, making it impossible to collect the gas quantitatively. No gas was evolved at the anode, which could be seen to undergo rapid electrolytic corrosion. The solid residue obtained after evaporation of the solvent and removal of the soluble ammonium trinitride by treatment with water, was found to consist of silver trinitride. The electrochemical efficiency has been calculated on the theory that AgN_3 was the sole product of corrosion in this case.

Expt. 7.—The cadmium wire which served as the anode in Expts. 7 and 8 extended to a depth of 8 cm. below the surface of the electrolyte. No corrosion was observed to take place before the circuit was closed. The electrolysis was carried on through a period of 40 minutes, during which no evolution of gas took place at the anode. A heavy, white deposit was formed at this electrode, however, and a slight deposit of black material, probably finely-divided metallic cadmium, appeared at the cathode.

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[1] Dennis and Isham, THIS JOURNAL, 29, 19 (1907).

[2] [illegible]

Expt. 8.—In continuation of Expt. 7 the electrolysis was conducted until the cathode deposit extended beyond the cathode tube, making impossible the quantitative collection of the gas liberated at the cathode. The white anode product was found to be stable in the air at ordinary temperatures, but was found to explode when heated. Treated with a solution of ferric chloride it showed the usual red coloration indicative of the presence of the trinitride ion. After it had been washed with water until the filtrate no longer gave evidence of this ion, a residue was obtained which contained N_3 and which exploded on heating This was soluble in hydrochloric acid, in hydronitric acid, and in ammonium trinitride solutions, and the resulting solutions yielded cadmium sulfide when treated with hydrogen sulfide. The anode product was probably either an ammonated cadmium trinitride, or an ammono-basic cadmium trinitride formed by ammonolysis of the original CdN_6 quantitatively produced by the action of N_3 upon the metallic anode.

Expt. 9.—A thin sheet of aluminum 0.75 cm. wide was employed as the anode. This was immersed to a depth of 8 cm. in the electrolyte. The electrolysis was allowed to proceed for two hours, during which a bulky, yellowish brown deposit accumulated at the lower end of the anode. On the upper part of the anode a very firm and coherent black coating of somewhat iridescent appearance was formed. This was presumably of identical composition with the yellowish deposit, but of very different physical form and compactness. The deposit was found to be non-explosive, and to contain no N_3. It was insoluble in water, but dissolved readily in a solution of sodium hydroxide. The resulting solution yielded flocculent aluminum hydroxide when boiled with ammonium chloride.

Expt. 10.—The electrolysis was effected under conditions similar to those prevailing in the preceding experiment. The residue obtained after vaporization of the liquid ammonia from the electrolyte was washed on the filter with successive 10 cc. portions of water, and the filtrate was in each case treated with ferric chloride. The ammonium trinitride was completely removed by the first 3 washings and in subsequent portions of the wash water no indications of N_3 in appreciable amount was obtained. The residue was found to be non-explosive, and to contain no N_3. It was found by the usual tests to be aluminum hydroxide.

Expts. 11 to 14.—For use in these 4 experiments a larger electrolytic cell was constructed, in which no provision was made for collection of could be prepared in larger quantity, and under conditions of lower and more nearly uniform anode current density. The product was obtained in the form of a fairly compact, though brittle, scale usually of an iridescent steel blue or black appearance. On the back of the electrode, where the current density was very low, a thin, coherent black coating identical with that described under Expt. 9 was deposited. This coating could be removed from the metal only with considerable difficulty

A curious phenomenon was observed in two cases during the removal of the loosely adherent scale from the front side of the anode. Almost immediately after the material was first exposed to the air, a spontaneous evolution of heat took place, accompanied by the appearance of a small quantity of smoke-like fumes. For the reason that this product is unstable in the air, no definite conclusion can be reached concerning its composition on the basis of the work herein described. Further work upon this problem has been carried out by other investigators in this laboratory, whose results will be published in the next article of the current series.

After the electrolysis had been in progess for some time, a deposit began to form upon the cathode in each of these experiments. This was originally of a dark appearance, but it faded to a dull gray color after the ammonia had been allowed to vaporize from the cell

Expt. 15.—The anode consisted of a strip of sheet lead 1.5 cm. wide. This was as usual immersed in the electrolyte to a depth of 8 cm. The duration of the electrolysis was for 30 minutes. No gas was evolved at the anode. A dark, loosely-adhering solid was formed at the anode, and a deposit, presumably of metallic lead, accumulated upon the cathode.

Expt. 16.—The material deposited upon the anode during this experiment, in which the conditions prevailing in Expt. 15 were duplicated, was found to explode on heating. It dissolved slightly in cold, and quite readily in hot water. The solution showed the characteristic reactions of lead salts and of trinitrides. The conclusion that the deposit consisted of lead trinitride, PbN_6, was substantiated by the calculated corrosion efficiency, and by the absence of any evolution of gas at the anode.

Expt. 17.—An antimony rod 0.5 cm. in diameter extending 8 cm. into the solution was used as the anode in this and the following experiment. The electrolysis covered a period of 30 minutes. No gas was evolved at the anode. A yellow solid was deposited upon the anode, and dropped from it at intervals.

Expt. 18.—The electrolysis was in this case continued for one hour. The yellow product that accumulated upon the anode was found to explode on heating. A portion of this solid was washed upon the filter with successive 10 cc. portions of water. Hydrolysis took place, with the result that hydronitric acid was found in the filtrates, while the color to be non-explosive, and to contain no N_3. When dissolved in hydrochloric acid this material showed the characteristic reaction of antimony compounds toward hydrogen sulfide. The anode corrosion efficiency was calculated on the assumption that antimony trinitride, $Sb(N_3)_3$, was formed at the anode.

Expt. 19.—An iron anode made of 20 strands of piano wire woven together was employed in Expts. 19 and 20 It was immersed to a depth of 7 cm. in the electrolyte, and was allowed to stand for two hours before the circuit was closed. No evidence of chemical action was observed. As soon as the current was turned on, however, the deep red color of ferric trinitride appeared in the neighborhood of the anode. Gas was evolved at the anode, but not so rapidly as at the cathode. The electrolysis was continued for 80 minutes.

Expt. 20.—The electrolysis was in this case allowed to proceed for 105 minutes. The solution assumed a deep red color, and a small amount of a dark colored substance was deposited upon the cathode. This was soluble in nitric acid, and the solution obtained showed the characteristic tests for iron. Vaporization of the liquid ammonia from the deep red electrolyte resulted in the formation of a brownish red residue. This was found by test to be in all probability an ammono-basic ferric trinitride, the exact composition of which was not determined.

Expt. 21.—A thin strip of nickel 0.25 cm. wide constituted the anode used in this and in the following experiment. This anode extended into the liquid to a depth of 8 cm. The electrolysis covered a period of one hour. Gas was evolved at the anode. A pink deposit gradually formed at this electrode, dropping off from time to time, and in part redissolving in the liquid, to which it imparted a decided brownish red coloration. The solid was found to explode on heating. On treatment with water the substance turned green, and gradually dissolved, forming a green solution, from which later a heavy green precipitate settled out. This precipitate was found to be explosive, and to contain nickel and N_3. It was undoubtedly a basic nickel trinitride formed by hydrolysis of the nickel trinitride, or possibly ammono-basic nickel trinitride formed in the cell. The washed residue differed from the original deposit in that it was insoluble in water and in ammonium trinitride solutions.

Expt. 22.—The electrolysis was continued over a period of 74 minutes. The observations made were corroborative of those described in the preceding paragraph. A very faint deposit was formed on the cathode in both of these experiments.

Summary.

In the present article are recorded the results of a series of experiments upon the behavior of various metallic anodes in a liquid ammonia solu-

It has been shown that copper anodes undergo electrolytic corrosion to an extent indicating the formation of some cuprous trinitride, CuN_3, with the cupric trinitride CuN_6 formed as the main product. No gas was liberated at the anode.

With silver, cadmium, lead, and antimony anodes, the corrosion resulted in the formation of the normal trinitrides AgN_3, CdN_6, PbN_6, and SbN_9, without liberation of gas at the anode. The corrosion efficiency as calculated on the basis of the quantitative formation of these compounds was found to be slightly in excess of 100%. This is probably not attributable to ordinary experimental error, but either to a slight mechanical or chemical corrosion, or else to a tendency toward the formation of unstable compounds containing the metals in a lower state of valence.

The aluminum, iron, and nickel anodes were found to undergo corrosion accompanied by liberation of nitrogen gas, as the result of which the efficiency fell far below 100%. The aluminum anode became coated with a bulky, pyrophoric scale of varying color and texture. Deep red ferric trinitride, FeN_9, was obtained in solution when the iron anode was employed, but this product was ammonolyzed, yielding an ammono-basic ferric trinitride. Upon the nickel anode a pink deposit, presumably an amono-basic nickel trinitride, was formed.

ITHACA, N. Y.

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF THE MIDVALE STEEL AND ORDNANCE COMPANY.]

AN ELECTROMETRIC METHOD FOR THE DETERMINATION OF FERROCYANIDES DEPENDING ON A CHANGE IN OXIDATION POTENTIAL.

BY G L. KELLEY AND R. T. BOHN.

Received August 16, 1919

In connection with some work in this laboratory, it became necessary to analyze potassium ferrocyanide solutions accurately. The oxidation of hydroferrocyanic acid by excess of iodine followed by titration with thiosulfate in the presence of alkali bicarbonate as proposed by Rupp and Scheidt[1] has been shown to be inaccurate.[2] Knublauch[3] titrates a sulfuric acid solution of the salt with copper of zinc sulfate, using a ferric salt as indicator. Smith's electrolytic method[4] would not distinguish between ferro- and ferricyanide ion if such were necessary. DeHaen[5] titrated a sulfuric acid solution with permanganate, but the difficulty of determining the end-point in a yellow solution of ferricyanide is manifest. DeHaen recommends standardizing permanganate against pure potassium ferrocyanide. We could not use the hydrated salt for this purpose because of efflorescence, and when dried at 120°, even in a stream of dry carbon dioxide, decomposition amounting to 8 to 15 parts in 10,000 occurred. Having observed that a sharp change in potential occurred during the titration of ferrocyanide with permanganate immediately before the color of the permanganate appeared, we undertook the study of the end-point.

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[1] *J. Soc. Chem. Ind*, 21, 1099 (1902).

[2] Sutton, *Volumetric Anal.*, 10th Ed., p. 217.

[3] *Ibid.*, p. 219.

[4] *Electro-Analysis*, 5th Ed., 1912, p. 302.

The change in oxidation potential has been used by Crotogino[1] in titrating halogens with permanganate, by Hildebrand[2] in the titration of chromates, by Forbes and Bartlett in the titration of ferrous[3] and chromous[4] salts, and by Kelley and others in the titration of vanadates,[5] chromates,[6] and permanganates.[7] Crotogino,[8] using a platinum black electrode, observed that the potential of the cell Pt — $K_4Fe(CN)_6$ — N Hg_2Cl_2 is 0.155 volt, while we observed the same cell to show a potential ranging from 0.20 to 0.41 volt, using a bright platinum electrode. The difference in the potential of the cell depends upon the nature of the solutions with which the electrode has been in contact, the amount of acid present, and the temperature We believe the electrometric titration of ferrocyanides to be new.

Our apparatus consisted in part of a bright platinum wire which served as a platinum electrode, a normal calomel electrode connected with a reservoir solution to permit flushing the tip of the electrode, and a glass stirrer operated by a motor. These two electrodes dipped into the solution which was to be titrated. The e. m. f. of this cell was balanced against a variable fraction of the e. m. f of a pair of dry cells. This was compared with a standard cell so that actual potentials for this cell could be read. A potentiometer manufactured by Leeds and Northrup was used for this purpose. It was possible to read 0.1 millivolt and to estimate to 0.01 millivolt. The weights, burets, and flasks were carefully standardized.

To study the character of the end-point, we at first employed a 0.005 N solution of permanganate and a solution of ferrocyanide of corresponding strength. As would be expected a gradual increase in potential occurs during the oxidation of ferrocyanide, due to the increase in concentration of ferricyanide ion, but this does not interfere with the detection of the end-point, the appearance of which is attended by a large change in potential. This last change is due to the presence of permanganate ion. Table I shows such titration In the example given, per-

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[1] *Z. anorg. Chem.*, 24, 225 (1900).

[2] This Journal, 35, 869 (1913).

[3] *Ibid.*, 35, 1527 (1913).

[4] *Ibid.*, 39, 1145 (1917).

[5] *Ibid.*, 38, 341 (1916).

[6] *J. Ind. Eng. Chem.*, 8, 719 (1916).

[7] *Ibid.*, 10, 19 (1918).

TABLE I

Titration of Potassium Ferrocyanide and Permanganate Solutions Approximately 0 005 *N* Volume 250 cc 40 cc of Sulfuric Acid (Sp Gr 1 58)

Temperature, 25°

$K_4Fe(CN)_6$ Cc	$KMnO_4$ Cc	Change Cc	E M F *Millivolts*	Change *in Mv*	Time *Min*	Total change *in Mv*
52 07	0	0	412	0		
	49 18	49 18	522	110		
	49 38	0 20	524	2		
	49 68	0 30	525	1		
	51 95	2 27	570	45		
	52 15	0 20	583	13		
	52 25	0 10	590	7		
	52 45	0 20	619	29		
	52 55	0 10	648	29	1	
			662	14	2	
			671	9	3	
			680	9	4	
			687	7	5	68
	52 60	0 05	705	18	1	
			710	5	2	
			720	10	3	
			730	10	4	
			739	9	5	52 end point
			748	9	6	
			770	22	10	
	52 64	0 04	780	10	1	
			788	8	2	
			796	8	3	
			800	4	4	
	54 11	1 47	926	126		
52.77		0 70	928	2		
53 41		0 64	912	16		
53 46		0 05	904	8	1	
53 51		0 05	896	8	1	
53 56		0 05	882	14	1	
			872	10	2	
			863	9	3	
			855	8	4	
			845	10	5	51
			836	9	6	
53 61		0 05	818	18	1	
			806	12	2	
			780	26	4	
			769	11	5	67 end-point
			758	11	6	
			702	56	12	

manganate was added to the end-point, then in excess. The end-point was then found by adding ferrocyanide, followed by an excess of this solution. The end-point was taken as the point of greatest potential change in 5 minutes for each like volume of titrating solution added. The two titrations gave identical results, although differences of the order of 3 to 5 parts in 1,000 were sometimes noted, especially with the amount of sulfuric acid used in this experiment.

Having determined the nature and delicacy of the end-point, we proceeded to work with stronger solutions, using for this purpose solutions of permanganate and ferrocyanide, which were approximately 0.05 *N*. One cc. of the permanganate solution by standardization against Bureau of Standards sodium oxalate was found to be equivalent to 0.003373 g. of oxalate or 0.02127 g. of hydrated potassium ferrocyanide.

The next step in our study of this method was the effect of the concentration of sulfuric acid. From the work of Crotogino,[1] one would expect a high concentration of acid to produce a high potential. This seems to be supported by other work which we have done. Obviously the lower limit of sulfuric acid concentration is that necessary to keep the products of reaction in solution. The upper limit is regulated by the fact that high concentrations of sulfuric acid cause interfering side reactions. The side reactions referred to are the decomposition of ferricyanide by sulfuric acid, giving rise to hydrocyanic acid as one of the products followed by reaction with permanganate. The occurrence of such side reactions was indicated in a variety of ways which are summarized below:

1. The increased consumption of permanganate when the titration was carried out by adding ferrocyanide to a permanganate solution. In this case a high concentration of permanganate was available for reaction with the decomposition products of the ferricyanide, as it was formed.

2. The amount of permanganate consumed in excess of the theoretical quantity increased with the concentration of permanganate, sulfuric acid and ferricyanide, and with an increase in temperature. When ferrocyanide was titrated with permanganate, this effect was not noticeable, even when the concentration of sulfuric acid was high, probably because the speed of the reaction between ferrocyanide and permanganate was so much greater than that between permanganate and the decomposition products of the ferricyanide. When the concentration of sulfuric acid was low, the consumption of permanganate on titrating this with ferrocyanide was normal. 2.5 cc. of sulfuric acid (sp. gr. 1.58) in a volume of 250 cc. of solution required two parts in one thousand more of permanganate when the ferrocyanide was added to the permanganate, than when the reverse operation was performed. With 5 cc. of acid, the difference was 3 parts in 1,000, but with 40 cc. of acid, it rose to 7 parts.

The presence of ferricyanide in addition to that produced in the reaction had a marked effect when the ferrocyanide solution was added to a solution containing ferricyanide, together with permanganate and 40 cc. of sulfuric acid. It had almost no effect when the sulfuric acid present was 2.5 cc.

3. The presence of ferricyanide in ferrocyanide solution had almost no effect upon the titration of the ferrocyanide with permanganate in all moderate concentrations of sulfuric acid

4. On warming a solution of ferricyanide containing sulfuric acid, the odor of hydrocyanic acid could be detected.

5. On titrating a warm solution of permanganate and sulfuric acid with ferrocyanide, the consumption of permanganate was too large.

The foregoing statements indicate that error will follow the use of concentrations of sulfuric acid greater than 5 cc. in 250 cc. volume when permanganate is titrated with ferrocyanide, and indicates likewise that some danger attends the use of the higher concentrations of sulfuric acid in the reverse titrations These statements are illustrated, in part, in Table II.

TABLE II

Effect of Temperature, Sulfuric Acid and Potassium Ferricyanide on the Titration of Ferrocyanide with Permanganate and on the Reverse Titration

Volume 250 cc Solutions Approximately 0.05 *N*

Temperature 25°

H_2SO_4 sp. gr. 1.58 Cc.	Solution titrated	Potassium ferrocyanide added G.	Permanganate ferrocyanide ratio
2.5	$KMnO_4$	none	1.011
2.5	$K_4Fe(CN)_6$	none	1.009
5.0	$KMnO_4$	none	1.011
5.0	$K_4Fe(CN)_6$	none	1.008
40.0	$KMnO_4$	none	1.016
40.0	$K_4Fe(CN)_6$	none	1.009
2.5	$KMnO_4$	1.5	1.008
2.5	$K_4Fe(CN)_6$	1.5	1.009
40.0	$KMnO_4$	none	1.035[1]
40.0	$KMnO_4$	1.0	1.102
40.0	$K_4Fe(CN)_6$	1.0	1.010

Table II shows titration of 0.05 *N* solutions with 2.5 cc. and 40 cc. of sulfuric acid present. On comparing these titrations with those obtained on titrating 0.005 *N* solutions with 40 cc. of sulfuric acid present, as shown in Table I, it will be noted that the change of potential is much greater near the end-point when the stronger solutions are used. With 0.05 *N* solutions it is not necessary to wait more than two minutes to determine the end-point. Table III also exhibits the favorable influence of a low concentration of sulfuric acid on this titration.

TABLE III.

Titration of Potassium Permanganate and Ferrocyanide Solutions, Approximately 0.05 *N*. Volume 250 cc. Temperature 25°.

$K_4Fe(CN)_6$ Cc	$KMnO_4$ Cc.	Change in cc.	E. M. F. millivolts	Change in mv	Time. Min	Total change
49.25	0	0	250	(2.5 cc. H_2SO_4 Sp gr 1.58)		
	49.18	49.18	505	255		
	49.40	0.22	506	1		
	49.56	0.16	515	9		
	49.64	0.08	532	17		
	49.67	0.03	598	66	1	
	.....	.....	650	52	2	
	. .		704	54	3	
	..	. .	753	49	4	221
	49.87	0.20	850	97		
49.25	0	0	365	(40 cc. H_2SO_4 Sp gr 1.58)		
	49.18	49.18	583	218		
	49.28	0.10	590	7		
	49.38	0.10	600	10		
	49.48	0.10	607	7	1	
	49.57	0.09	618	11	1	
	49.62	0.05	629	11	1	
	49.66	0.04	652	23	1	
	49.70	0.04	718	66	1	
	.	. . .	732	14	2	
	..	.	745	13	3	
		.	761	16	4	100

One of the products of the reaction is manganous sulfate. We investigated the effect of increasing the concentration of this salt. As a result we learned that a moderate increase in concentration over that resulting from the reaction caused a precipitate of manganous ferricyanide, which coated the electrode and seriously interfered with the titration even when the concentration of sulfuric acid was high. This suggests a limit to the amount of ferrocyanide which can be titrated in this volume. This limit corresponds to about 50 cc. of a 0.05 *N* solution, and may not be greatly exceeded.

Large concentrations of hydrochloric acid reacted with the permanganate. With less than one cc. of conc. hydrochloric acid in a volume of 250 cc., no difficulty was experienced when ferrocyanide was titrated with permanganate. It is thus shown that chlorides in moderate amount do not interfere.

The substitution of potassium dichromate as the oxidizing agent for potassium permanganate was unsuccessful. This reaction requires time and high temperature for its completion. It was therefore abandoned.

The titration shown in the tables given in this paper involved about 50 cc. each of the solutions. We have also titrated smaller volumes, solutions to be the same within the same limit of error in measuring, whether dilute or strong solutions were used. The method is, therefore available for the determination of very small amounts of ferrocyanide, and in this respect it corresponds with the determination of small amounts of chromate by electrometric titration with ferrous sulfate as described by one of us elsewhere.[1] The question as to the correctness of the end-point which we have taken is only partly answered by the approximate coincidence of the electrometric end-point and the appearance of the color of the permanganic acid because of the difficulty in noting the point at which the change of color occurs. We believe, however, that the close agreement between end-points reached by titrating ferrocyanide with permanganate and permanganate with ferrocyanide is further and confirming evidence of the correctness of the end-point and that it shows that there is no need for a blank correction in this titration in work corresponding to an accuracy of one part in 500.

Method for Determining Ferrocyanide.

About one g. of potassium ferrocyanide in 250 cc. of water and 2.5 to 5.0 cc. of sulfuric acid of sp. gr. 1.58, may be titrated with 0.05 *N* permanganate. The permanganate should be standardized against Bureau of Standards sodium oxalate. Ferricyanide does not interfere. The titration should be performed by adding the permanganate slowly with constant mechanical stirring to the solution of ferrocyanide. A small precipitate may form, but this redissolves. The electrometric apparatus must be one which will indicate changes in potential of the order of one millivolt. This condition is fulfilled by the apparatus described by Hildebrand,[2] and, with the addition of a voltmeter, by the apparatus described by one of us.[3] As the end-point is approached, the permanganate should be added dropwise, and time allowed for the completion of the reaction. This is illustrated in Table I. The end-point is taken as the point of greatest change in potential, corresponding to the addition of equal amounts of the permanganate solution. Should too much permanganate be added, the end-point may be approached from the opposite direction by adding a standard solution of ferrocyanide. The concentration of permanganate in this case is so low that the cautions given elsewhere in this paper concerning the danger of titrating permanganate with ferrocyanide are not applicable. There is even some advantage in titrating in this way in that in this titration, as in most others, depending upon a change in oxidation potential, the sharper end-points are obtained when the electrode is in contact with the oxidizing solution. Chloride in amounts equivalent to one g. of sodium chloride do not interfere. Any salts which under the conditions produce a precipitate with either ferro- or ferricyanide interfere.

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[1] *J. Ind. Eng. Chem.*, 9, 780 (1917).

Nicetown, Philadelphia, Penna.

[Contribution from the Department of Chemistry of Princeton University.]

THE VAPOR PRESSURES OF MERCURY IN THE RANGE 120° TO 250°.

By Alan W. C. Menzies

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In a former paper[1] it was pointed out that the values found by various observers for the vapor pressures of mercury are astonishingly discordant. For this and for other reasons there mentioned, the vapor pressures were redetermined at that time over the temperature range 250–435°, using the static isoteniscope.[2] In the present paper a report is made of measurements covering the range 120–250°, using two McLeod gages.

The Existing Data.—The more important observations within the range stated are collected in Table I, in which the observers' names are

Table I

Data of Other Investigators

Observer	Temp	Press obs mm mercury	Press calc from equation R mm mercury	Press diff Calc − Obs mm mercury	$\frac{P \text{ calc}}{P \text{ obs}} \times 100.$
G	248	71.39	70.29	−1.10	101.6
G	245	68.42	64.89	−3.53	103.0
Y	236.9	51.85	52.03	+0.18	99.6
G	236	51.58	50.72	−0.86	101.7
G	230.5	46.49	43.21	3.28	107.5
G	224.5	38.82	36.56	−2.26	106.2
G	207	21.07	21.53	+0.46	97.9
H	206.9	22.58	21.47	−1.11	105.2
H	203.0	20.35	18.97	−1.38	107.3
H	190.4	12.89	12.54	−0.35	103.0
G	188	12.51	11.56	−0.95	108.2
H	184.7	11.04	10.32	−0.72	107.0
Y	183.8	9.94	10.00	+0.06	99.4
Y[*]	183.7	9.85	9.97	+0.12	98.8
RY	183.4	9.87	9.87	−0.00	100.0
H	177.4	8.20	7.98	−0.22	102.7
G	176.5	8.22	7.73	−0.49	106.4
H	165.8	5.52	5.22	−0.30	104.3
G	157.5	3.93	3.72	−0.21	105.7
H	154.2	3.49	3.33	−0.16	104.9
G	129	1.00	1.14	−0.14	87.4

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[1] Smith and Menzies, This Journal, 32, 1434 (1910).

[2] This Journal, 32, 1412 (1910).

abbreviated thus, Young[1] Y, Ramsay and Young[2] RY, Hertz[3] H, Gebhardt[4] G. The "calculated" values are those given by the equation "R" published in 1910,[5] and yield, at least, a smooth curve to serve for purposes of comparison. The amounts of discrepancy are tabulated in the fourth column in mm. of mercury, and, in the fifth column, are made evident by a percentage comparison.

The Method Employed.—The static isoteniscope is not especially well suited for the measurement of the rather low vapor pressures with which we are here concerned, and an entirely new plan was therefore adopted. Two McLeod gages, G and G′ in the diagram (Fig. 1), of suitable capacities were constructed and calibrated. These were connected with each other and with the reservoir A and also, through a mercury seal, with a source of pure dry hydrogen and with a vacuum pump. The gage G′ was completely immersed in an oil bath, fitted with an arrangement for violent stirring,[6] while the gage G and the reservoir A were immersed in water baths at room temperature. By successively admitting and pumping out dry hydrogen, heating the glass meanwhile, the apparatus could be filled with this gas, whose pressure could finally be made whatever was desired prior to closing the mercury seal. If not already done to assist in the removal of adsorbed substances, the gage G′ was raised to the desired temperature, ascertained by a completely immersed mercurial thermometer of known corrections. Both gages were then operated simultaneously, and, because of the condensation on compression of the saturated mercury vapor in G′, gave different readings, from which the required vapor pressure could be calculated. In

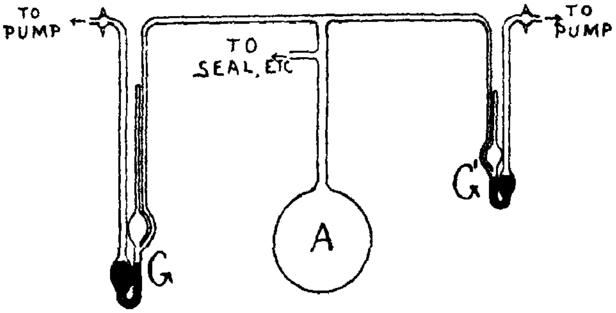

Fig 1.

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[1] *J. Chem. Soc.*, 59, 629 (1891).

[2] *Ibid.*, 49, 37 (1886).

[3] *Ann. Physik*, [3] 17, 193 (1882).

[4] *Ber. physik. Ges.*, 7, 184 (1905); *Dissertation*, Erlangen, 1903.

[5] *Loc. cit.*

all cases, equilibrium had already become established even at the first reading.

This method is applicable, not only to mercury, but to other substances whose saturated vapors may be suitably introduced into the G′ gage over either mercury, fusible metal or other liquid.

Reduction of Observations.– As identical results for the vapor pressure of mercury were obtained with different pressures of hydrogen, it may be assumed that, in these experiments, the total pressure P in the cold gage is identical with that in the hot gage before the operation of the gages, within the experimental error. Because the gas pressures measured are not negligibly small as compared with the pressure due to the mercury column of the gage, the ordinary formula used for McLeod gages will not apply strictly Instead, if V is the total volume of the gage, v the volume of the compressed gas trapped in the gage capillary, l the height in mm. of the mercury column chiefly responsible for the compression, and P the pressure in mm of mercury of the gas in the reservoir A, which it is desired to measure, one may state $P/(l + P) = v/V$; or $P = lv/(V - v)$. This equation was used for the cold gage G, where the vapor pressure of mercury was almost negligible.

In the hot gage G′, the pressure P, prior to the act of compression, is made up of [Hg] the vapor pressure of mercury and $[H_2]$ the partial pressure of hydrogen, whence $[H_2] = P - [Hg]$. After compression, the pressure in the gage capillary is made up of [Hg], as before, plus $[H_2] \times V'/v'$ and this total pressure is also equal to that of the mercury head l' plus P Thus

$$P + l' = [\mathrm{Hg}] + \{P - [\mathrm{Hg}]\} \times \frac{V'}{v'}$$

or,

$$[\mathrm{Hg}] = P - \frac{v'l'}{V' - v'} = \frac{lv}{V - v} - \frac{l'v'}{V' - v'},$$

which gives the required vapor pressure of mercury.

Precautions to Secure Accuracy.—The hot gage must be sufficiently compact in construction to make possible immersion in the oil bath; but the cold gage may be practically as large as desired. The cold gage reading can thus, ordinarily, be of much higher accuracy. Since the last equation above shows that the hot gage reading is to be subtracted from the cold gage reading to obtain the result, it will obviously be best to arrange to have the hot gage reading relatively rather small, thus reducing its errors to a secondary order. This can be effected by adjusting the hydrogen pressure in the apparatus to have a value not much larger than the anticipated vapor pressure. Again, it should be borne in mind that a McLeod gage reads most accurately for the highest pressures that it will record The operation of cutting off or trapping the gage gas should be performed very slowly. The readings of heights of mercury columns should, of course, be suitably reduced for temperature and gravitation. A small correction, based on equation "R," was applied to correct for the mercury vapor present in the cold gage.[1]

Measurements Made.—The mercury employed was purified by the customary methods.[2] There was no evidence that it dissolved hydrogen appreciably. In such a case as the present one, all that is necessary is the determination of a very few points. Thermometry in agreement to 0.1° with the 1914 scale of the Reichsanstalt was available only up to 200°, and the 3 points selected are, therefore, below this temperature. The "calculated" values in Table II below are those obtained from the equation

$$\log p = 9.9073436 - 3276.638/\theta - 0.6519904 \log\theta \qquad (R)$$

which was based on measurements between 250° and 435° and published in 1910.[3] The values in the fifth column, which give the percentage change in pressure that would be caused by a temperature change of 0.1°, are also derived from this equation. From the values of the pressure of hydrogen in the reservoir, tabulated under P, one can see that, in these experiments, the accuracy to be expected is greatest at 191.5° and least at 121.8°, for reasons mentioned in a preceding paragraph.

TABLE II.

Details of Observations

Temperature	Vapor pressure in mm mercury at 0°		$\frac{\text{Found}}{\text{Calc}} \times 100$	Percentage change of press per 0.1° calc from R	P.
	Found	Calc from R			
191.5°	13.02	13.02	100	0.34	14.28
150.0°	2.802	2.811	99.67	0.39	3.564
121.8°	0.829	0.823	100.75	0.47	1.738

At 191.5° the agreement between the found and calculated values is only apparently perfect, for the temperature scales concerned differ by several hundredths of a degree at this point.[4] This disagreement between the found and the calculated values, however, is in no case greater than the estimated experimental error.

Conclusions.

The measurements here reported, therefore, indicate that the vapor pressures of mercury between 120° and 250° may be represented, probably to within 1% of their own values, by the same equation "R," without the need of any modification meantime, that was adapted to fit the experimental values formerly found in the range 250° to 435°. The difference between the temperature scales employed in 1910 and in the present work is within the experimental error.

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[1] It should, perhaps, be mentioned that, at the pressures and compressions used, the divergence of hydrogen from the simple gas law gives rise to errors of an order here quite negligible. Possible systematic error is being further investigated.

[2] Cf. THIS JOURNAL, 32, 1439 (1910).

[3] *Ibid.*, 32, 1441 (1910).

[4] [illegible]

Measurements by this method may be extended to lower temperatures; and the precision here attained may be improved with respect to pressure as well as to temperature. But such further measurements by this method are perhaps unnecessary in view of the greater simplicity of another method, applicable to this and to many other cases, giving results which it is hoped will be published later.

Summary.

(1) A method adapted to the measurement of rather low vapor pressures has been described, involving the use of two McLeod gages, hot and cold, respectively.

(2) This method has been applied to the case of mercury, and it has been shown that the equation connecting pressure and temperature published in 1910 to cover the range 250° to 453° may be applied, without modification of its constants, over the range 120° to 250°.

Princeton, N. J.

[Contribution from the Chemical Laboratory of the University of California.]

POTENTIALS OF THE ZINC AND CADMIUM ELECTRODES.

By W. Grenville Horsch

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Normal electrode potential has been defined[1] as the electromotive force of a reversible electrode of the pure element against a solution in which the ion of the element is (hypothetical) molal. This paper presents determinations of the normal electrode potentials of zinc and cadmium referred to the potential of the normal hydrogen electrode as zero.

In a previous, unpublished research[2] a value for the electrode potential of zinc was obtained, based upon measurements of cells containing sulfate solutions as electrolytes. The electromotive force of cells of the type $\underline{Zn}: ZnSO_4: Hg_2SO_4: Hg$ was measured[3] where the zinc sulfate solutions ranged in concentration from 0.005 *M* up to 0.1 *M*. Using the method of calculation employed by Lewis and Lacey[4] to obtain the potential of the copper electrode, and their value of the electromotive force corresponding to the free energy of formation of mercurous sulfate, the value 0.76 volt was obtained as the potential of the zinc electrode. It was

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[1] Lewis, This Journal, 35, 22 (1913); 36, 1972 (footnote) (1914).

[2] W. G. Horsch, *Thesis* for the degree of S.M., Univ. of Calif., 1916.

[3]

Molal concn. of $ZnSO_4$ soln.,	0.005	0.010	0.020	0.030	0.070	0.100
Electromotive force,	1.5195	1.5144	1.5054	1.4988	1.4880	1.4830

[4] This Journal, 36, 804 (1914).

estimated that the value of the potential thus obtained might contain an error as great as 0.01 volt.[1]

Because of the unsatisfactory nature of mercurous sulfate, some other insoluble sulfate was sought, the properties of which made it more suitable for use in a reference electrode. The only substance appeared to be lead sulfate, which possesses the advantage of having $^1/_{10}$ the solubility of mercurous sulfate. Accordingly, experiments were tried, using electrodes consisting of solid lead sulfate in contact with a liquid containing 1% lead. Cells of the type $Hg: \underline{Hg_2OS_4}: ZnSO_4(0.04M); \underline{PbSO_4}Pb$(amalg.), were measured, in which two mercurous sulfate-mercury electrodes and two lead sulfate-lead electrodes dipped into the same intermediate vessel. The former two differed from each other by less than 0.0001 volt; the latter two differed by 0.0004 to 0.0010 volt. Moreover, the measurements were unsatisfactory for the further reason that the electromotive force of the cell fell off rapidly with the time; thus the electromotive force of the cell changed from 0.954 to 0.946 volt in 18 hours. Lead sulfate-lead against zinc in zinc sulfate solutions gave a continually rising electromotive force, while mercurous sulfate-mercury against zinc sulfate solutions remained constant over long periods. Even greater inconstancy was found by Lewis and Brighton[2] who used cells which consisted of hydrogen, sulfuric acid, lead sulfate in sulfuric acid, lead. The attempted use of an especially designed electrode in which the contact surface between the amalgam and the solution could be renewed continuously or at will proved unsuccessful. It was therefore evident that sulfates could not be employed in the cells if accurate values of the electrode potentials of zinc and cadmium were desired.

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[1] The uncertainty of this value is attributed to the mercurous sulfate. Thus, measurements of the electromotive force of the cell $\underline{Zn}$, $ZnSO_4$, Hg_2SO_4, Hg at two different concentrations of zinc sulfate solution should enable us to calculate the free energy of dilution of zinc sulfate solution. The free energy of dilution may be calculated also from freezing-point data. The values obtained by the two methods (using freezing-point data of H. Hausrath (*Ann. Physik*, [4] 9, 550 (1902)), do not agree, but differ by an amount corresponding to 0.005 to 0.008 volt. This discrepancy is greater than can be attributed to the error in either the freezing-point data or the electromotive-force measurements, and is due partly to the solubility of mercurous sulfate. The solubility in pure water is 0.0013 *M* at 25°, so that the amount of sulfate ion contributed by the mercurous sulfate becomes an important factor in the dil. zinc sulfate solutions. Mercurous sulfate turns yellow and then light brown, as the zinc sulfate solution with which it is in contact becomes more and more dilute. The action is hastened by light, but is prevented by a small concentration of acid. According to Wright and Thompson (*Phil. Mag.*, [5] 19, 29 (1885)), zinc sulfate solution renders the mercurous sulfate more soluble; for example, in a saturated solution of zinc sulfate, the mercurous sulfate had 3 times its solubility in pure water. These considerations indicate that in dil. sulfate solutions the activity of the zinc ions is affected by the presence of the mercurous sulfate. In obtaining the normal potential against hydrogen the calculation was based on the assumption that the mercurous sulfate had the same thermodynamic properties in acid as in dil. zinc sulfate solution.

[2] THIS JOURNAL, 39, 1908 (1917).

Experiments were tried next with chlorides. Measurements of cells of the type $\underline{\text{M}}:\text{MCl}_2:\underline{\text{AgCl}}:\underline{\text{Ag}}$, (A) and $\text{H}_2:\text{HCl}(0.01\,M):\underline{\text{AgCl}}:\underline{\text{Ag}}$, (B) where $\underline{\text{M}}$ represents zinc or cadmium, were found to give entirely satisfactory results in respect to constancy and reproducibility. It is these measurements which form the basis of the electrode potentials which are presented in this paper. The electromotive force of (B) enables us to calculate the electromotive force corresponding to the free energy of formation of AgCl in (hypothetical) molal H^+ and Cl^-. This value, together with the electromotive force of (A) in a solution so dilute that we may get the activity of M^{++}, enables us to calculate the potential of $\underline{\text{M}}$ against (hypothetical) molal M^{++}.

Work of Other Investigators.—H. Jahn[1] determined the electromotive force of the cell Zn (amalgamated rod) ZnCl_2 (c); $\underline{\text{AgCl}}$; $\underline{\text{Ag}}$, in concentrations of ZnCl_2 from 0.556–2.22 M; these will be tabulated along with the author's own values for zinc. H. M. Goodwin[2] measured the electromotive force of concentration cells of the type

$$\underline{\text{Cd}},\ \text{CdCl}_2\ (c_1);\ \underline{\text{AgCl}},\ \underline{\text{Ag}},\ \underline{\text{AgCl}};\ \text{CdCl}_2\ (c_2),\ \underline{\text{Cd}}$$

$$\underline{\text{Zn}},\ \text{ZnCl}_2\ (c_1);\ \underline{\text{AgCl}},\ \underline{\text{Ag}},\ \underline{\text{AgCl}};\ \text{ZnCl}_2\ (c_2),\ \underline{\text{Zn}}$$

in a few concentrations ranging from 0.001–0.2 M. The electromotive forces of a few cells in which Cd was placed against $\underline{\text{AgCl}}$, $\underline{\text{Ag}}$ in CdCl_2 were measured by Wright and Thompson[3] and by E. Biron and B. Afanassjew.[4] Those of the former were all carried out in solutions of concentration greater than about 0.05 M. Details of the work of the latter two investigators could not be obtained.

Apparatus.

Potentiometer.—Measurements of electromotive force were made with a potentiometer of the decade-box type, which has been in use in this laboratory for several years. A complete description is given in a recent paper by Lewis, Brighton and Sebastian.[5] The potentiometer and all conductors connected therewith were thoroughly protected from stray electric effects by a conducting shield, according to the method recommended by White.[6] By the use of paraffined glass tubes for supports, all parts of the potentiometer system, including wires leading to the cells and to the galvanometer, possessed a high degree of insulation.

Oil Bath.—All the cells when being measured were immersed in an oil bath which was maintained at a temperature of 25° ± .01 by means of an electric heater and an electrically operated thermostat.

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[1] *Wied. Ann.*, 28, 21–43, 491–7 (1886).

[2] *Z. physik. Chem.*, 13, 577–656 (1894).

[3] *Phil. Mag.*, [5] 19, 106 (1885).

[4] *J. Russ. Phys. Chem. Soc.*, 41, 1175–82 (1909).

[5] THIS JOURNAL, 39, 2246 (1917).

Cells.—Two types of cell were used. For the measurements with the more concentrated electrolytes was employed the ordinary "half" cell, so common in electromotive force work. It consisted of a glass tube about 2 cm. in diameter and 15 cm. in height, closed at the bottom, and with a side arm opening from it near the middle. The metal of which the e. m. f. was desired was placed in the bottom of the tube and contact made by means of a sealed-in platinum wire. The slight solubility of silver chloride, and the form of the silver-silver chloride electrode (to be described presently) made it possible to insert the latter in the upper part of the same chamber with the zinc or cadmium. The "half" therefore became a complete cell in itself. For the purpose of intercomparison several of these units could be connected, by means of the side arm, with a common intermediate vessel. Where this was unnecessary, the side arm was closed to prevent evaporation and was used merely as a means of support.

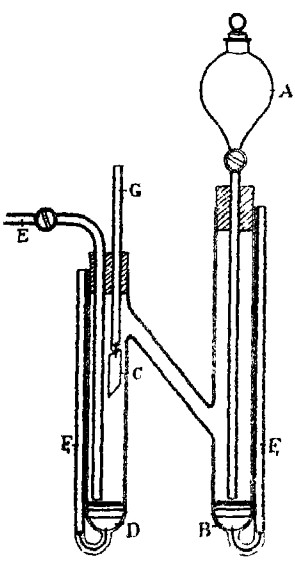

Fig. 1

For work with dilute solutions, a special cell (Fig. 1) was designed which permitted the circulation of fresh electrolyte through it while it was in the oil bath. Each complete cell of this type carried two metal electrodes, B and D, and one silver-silver chloride reference electrode, C. A small supply of electrolyte, carried in the dropping funnel A, could be allowed to flow down when desired, washing, in turn, the electrode surfaces at B, C, and D, finally passing out through the waste-tube, E. Contact with the potentiometer leads was made by means of mercury placed in the tubes F_1, F_2, and G, in the lower ends of which platinum wires were sealed.

Preparation of Materials.

Standard Metal Electrodes.—Finely divided metals, cadmium and zinc, produced by rapid electrolysis of the chloride solution, were used. A rod of the pure metal served as anode, and a platinum spiral as cathode in this electrolysis. Varying the current density at which the metal was deposited had no effect on the electromotive force exhibited by the metal, except that with very high current density the deposited metal became [illegible] as to pack together and thereby prevent efficient washing.

wire the current employed was 0.25 to 0.50 ampere. The tree-like deposit was shaken from this cathode from time to time, and when sufficient amount had been obtained in the bottom of the beaker in which the electrolysis was conducted, it was removed and washed.

Liquid Amalgams of both zinc and cadmium were prepared. These contained 3.6% zinc and 4.6% cadmium, respectively. Weighed amounts of zinc (or cadmium) and mercury were enclosed in an evacuated tube and heated in a steam bath until the solid had dissolved. The mixture was shaken occasionally to hasten the process and after the solid had disappeared a thorough shaking was given to insure homogeneity. Cadmium amalgam gave excellent results in all concentrations of cadmium chloride solution from saturation down to 0.0001 *M*. The zinc amalgam prepared did not give a steady electromotive force in zinc chloride solution of any concentration. It was found, however, that finely divided zinc worked satisfactorily in solutions as dilute as 0.0003 *M*. Therefore, while there is no serious doubt as to the ability of zinc amalgam to give reproducible results, a study of its apparently anomalous behavior was given up, and the pure (spongy) zinc used directly.

Cadmium Chloride solutions were prepared by weighing out the proper amounts of water and of a stock solution of cadmium chloride of known concentration. This stock solution was prepared by dissolving very pure, crystalline cadmium chloride in "conductivity" water. The concentration was determined by 5 analyses, using the silver chloride precipitation method.

Zinc Chloride solutions were prepared likewise by diluting a stock solution of zinc chloride. In this case, however, pure zinc chloride was not available, so that a zinc chloride solution was prepared as follows· Pure hydrogen chloride was obtained by dropping pure, conc. sulfuric acid slowly into pure, conc. hydrochloric acid. The gas was absorbed in conductivity water until the concentration was about 0.5 molal. An excess of spongy zinc, carefully washed, was then added to this acid solution and the mixture warmed gently until no further zinc would dissolve. This solution reddened litmus slowly. The solution was then filtered to remove the excess zinc and the filtrate diluted to about 0.15 *M*, analyzed (as in the case of cadmium chloride), and employed as a stock solution.

Silver-Silver Chloride Electrodes were prepared according to the method already employed successfully by Brighton[1] working in this laboratory. Flat platinum gauze, about 2 × 1 cm., was fastened to the end of a platinum wire, which in turn was sealed into the lower end of a glass tube of about 4 mm. inside diameter. The gauze was plated with silver from a silver cyanide bath, and then the silver chloride formed as a dark deposit by using the silver as anode in a dil. sodium chloride solution to which a small amount of hydrochloric acid had been added

Experimental Results.

Amalgam *vs* Pure Cadmium.—Three samples of cadmium amalgam were taken, representing approximately the first, middle and last portions drawn from the storage tube The electromotive force of these against pure cadmium was obtained by measurements of a cell containing the amalgam in one arm and pure cadmium in the other, the electrolyte throughout being 0 5 *M* cadmium chloride solution[1] The finely divided cadmium did not give concordant or constant results in dil cadmium chloride solutions, but in 0 5 *M* concentration the agreement was excellent. The cells were kept in the bath from 2 to 5 days, and in each case the electromotive force varied by less than 0 0001 volt during the whole period The results are as follows

Portion	*E* in volts
First	0 0536
Middle	0 0534
Last	0 0533

Taking the average of these values we obtain

$$\text{Cd(amalgam)}\ \ \text{Cd}^{++}\ \ 2\text{Cl}^-\ \ \underline{\text{Cd}}\ \ E = -0\ 0534\ \text{volt.}$$

TABLE I

I M F of the Cell $H_2(p)$ HCl(0 01 *M*) AgCl Ag

Electrode	E^2 (observed) Volt	Barom Press (Mm Hg at 0°)	E^3 (corrected to 1 atm) Volt
1	0 4660	751 4	0 4666
2	0 4659	751 4	0 4665
4	0 4655	751 4	0 4661
4	0 4666	751 7	0 4670
5	0 4660	745 7	0 4665
5	0 4660	756 5	0 4665
6	0 4658	753 7	0 4663
6	0 4660	759 7	0 4664
6	0 4661	757 1	0 4666
6	0 4659	755 6	0 4664
7	0 4662	759 7	0 4666
		Mean value,	0 4665

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[1] The electromotive force should be independent of the concentration of Cd^{++}

[2] The electrodes were checked up several times at intervals of a few days *E* represents the mean of the values thus obtained

[3] The calculation of *E* (corrected to a hydrogen pressure of 1 atmosphere) given in Table I, was made as in the following example for Electrode No 1

E (observed) 0 4660 volt

Water vapor pressure at 25° = 24 mm

Actual hydrogen pressure = 751 — 24 = 727 mm

Correction = $E = RT/2F \ln 760/p = 0\ 0296 \log 760/727 = 0\ 0006$ volt

$E\ (p = 1\ \text{atm}) = 0\ 4660 + 0\ 0006 = 0\ 4666$ volt

Silver-Silver Chloride *vs.* **Hydrogen.**—All the silver-silver chloride electrodes had the same electromotive force within two- or three-tenths of one millivolt, when measured against hydrogen in 0.01 *M* hydrochloric acid. The results are presented in Table I, where *E* represents the e. m. f. of the cell $H_2(p)$; HCl(0.01*M*)[1] · $\underline{\text{AgCl}}$: $\underline{\text{Ag}}$.

Cadmium Amalgam *vs.* **Silver-Silver Chloride.**—Owing to the good agreement of the silver-silver chloride electrodes among themselves, it was unnecessary to correct the individual observations of e. m. f. of cadmium against silver-silver chloride for the deviation of the latter from the mean.

In Table II are presented the original observed e. m. fs. of the cell Cd(4.6% amalgam), $CdCl_2(c)$, $\underline{\text{AgCl}}$, $\underline{\text{Ag}}$, (E_1), and of the (calculated) e. m. fs. of the cell $\underline{\text{Cd}}$, $CdCl_2(c)$, $\underline{\text{AgCl}}$, $\underline{\text{Ag}}$, ($E_2 = E_1 - 0.0534$), the correction term being equal to the e. m. f. of pure cadmium against the cadmium amalgam.

Two or more electrodes always were measured in each concentration of cadmium chloride solution, and it is the mean value of these measurements which is given in the second column of Table II. The cadmium amalgams gave very concordant results in concentrations down to about 0.0005 *M*. The equilibrium value of the electromotive force was taken on very promptly (within 5 or 10 minutes after the cell was prepared and placed in the bath) and did not differ by more than 0.0005 volt from the initial value. This indicated that no appreciable amount of reaction took place between the electrode and the solution. Several cells were left in the bath over a period of 3 or 4 days, during which time they did not vary by more than 0.0002 to 0.0003 volt. In all cases the cells were emptied and refilled with electrolyte several times during the period of the experiment. Where the concentration was about 0.001 *M* or greater, the electromotive force was always reproduced after the refilling. In

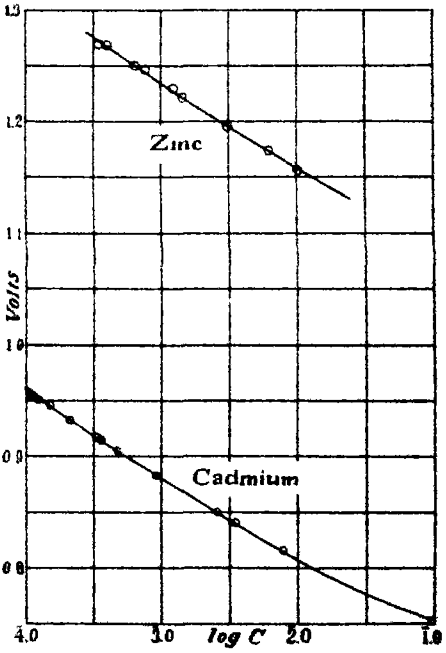

Fig 2.

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[1] The concentration of the hydrochloric acid used was actually 0.00999 *M*.

the very dilute solutions, say below 0.0005 M, the several cells did not agree more closely than 0.0005 to 0.0010 volt, and in successive fillings with fresh electrolyte the electromotive force was not reproduced any better than this.

The original observations, as given in Table II, when plotted against the logarithm of the concentration (see Fig. 2) lie on a smooth curve to which the points hold very closely down to a concentration of about 0.00025 M. Even below this concentration the maximum deviation of any of the points from the curve is less than 0.0012 volt, so that the least accurate portion of the curve, since it represents an average of the measurements, should give the electromotive force to nearer than 0.001 volt.

TABLE II

E. M. F. of the Cell: Cd(4.6 amalg.) : $CdCl_2(c)$: $\underline{AgCl}$: $\underline{Ag}$.

C ($CdCl_2$) mols per 1000 g of H_2O	E_1 (observed)	E_2 ($= E_1 + 0.0534$)
6.62	0.62203	0.67540
0.0995	0.6996	0.7530
0.0074	0.76305	0.81645
0.003519	0.7864	0.8398
0.002581	0.7958	0.8491
0.000924	0.8296	0.8830
0.000470	0.852	0.905
0.0003659	0.8614	0.9148
0.0003363	0.8644	0.9178
0.0002144	0.8803	0.9337
0.0001527	0.8926	0.9460
0.0001269	0.8978	0.9512
0.0001137	0.9011	0.9545
0.0001087	0.9023	0.9557
0.0001029	0.9060	0.9594

Zinc *vs.* Silver-Silver Chloride.—In the work with zinc the pure metal in the finely divided form was used directly. As a "standard" value for the e. m. f. of silver-silver chloride against hydrogen in 0.01 M hydrochloric acid, 0.4665 volt was taken. Whenever any of the silver-silver chloride electrodes used in these measurements differed from 0.4665, the corresponding reading was corrected by the proper amount. It has already been pointed out that the finely divided zinc was used instead of zinc amalgam because the amalgam gave unsteady values of electromotive force. Between two samples of the same amalgam the electromotive force varied in an erratic manner, rising and falling rapidly. The finely divided zinc gave a steady value, but left something to be desired in the way of reproducibility in the dilute solutions. For this reason the measurements were not carried out in solutions of zinc chloride more dilute than 0.0003 M, and in concentrations below 0.001 M the deviation of the individual observations from the mean is 0.002 volt. As in the case of the cadmium measurements, the cells were emptied and refilled several times with fresh zinc chloride solution, and each value given in Table III represents the mean of the value by at least two separate cells. Whether the silver-silver chloride was in the same tube with the metal (zinc or cadmium), or separated by an intermediate vessel or tube, made only two- or three-tenths of a millivolt difference in the case of the dilute solutions and an undetectable difference in the case of the more concentrated solutions. In Table III are presented the observed e. m. fs. of the cell $\underline{\text{Zn}}$; $ZnCl_2(C)$, $\underline{\text{AgCl}}$, $\underline{\text{Ag}}$. These values of E are plotted against log C in Fig. 2.

TABLE III

E. M. F. of Cell $\underline{\text{Zn}}$, $ZnCl_2(c)$, $\underline{\text{AgCl}}$, $\underline{\text{Ag}}$

C ($ZnCl_2$) mols per 1000 g. H_2O	E (observed) (Volts.)
0.01021	1.1558
0.006022	1.1742
0.003112	1.1953
0.001453	1.2219
0.001253	1.2289
0.000772	1.2475
0.000649	1.2497
0.0003995	1.2690
0.0003478	1.2701

In Table IV are presented three values by H. Jahn[1] to supplement those given in Table III. Jahn used an amalgamated zinc rod instead of pure zinc. Since, as pointed out by Richards and Lewis,[2] the difference in potential between pure zinc and its saturated amalgam is slight (only a few millivolts) the comparison is a fair one to make.

TABLE IV

Data of H. Jahn. E. M. F. of Cell $\underline{\text{Zn}}$, $ZnCl_2(c)$, $\underline{\text{AgCl}}$, $\underline{\text{Ag}}$

C ($ZnCl_2$) mols per 1000 g. H_2O.	E (observed) (Volts.)
0.566	1.0300
1.112	1.0171
2.22	0.9740

Activities of the Ions.

In solutions of bi-univalent salts the determination of the thermodynamic degree of dissociation is rendered difficult (1) because of factors which are identical with those appearing in the case of uni-univalent salts, although probably exaggerated in this case; (2) because of uncertainty regarding intermediate ions; and (3) because in the case of zinc and cadmium chloride there is also the possibility of another type of complex anion. Nevertheless, as infinite dilution is approached all of these factors of uncertainty disappear, and if accurate electromotive-force measurements could be made in very high dilution the value of the normal electrode potential could be calculated at once. At high dilutions, however, not only does the solubility of the material used in the electrode (such as mercuric sulfate or silver chloride) produce some uncertainty, but other errors of unknown origin become highly exaggerated.

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[1] *Loc. cit.*

[2] *Proc. Am. Acad.*, **34**, 87 (1898).

In every experimental study of electrode potentials the attempt is made to obtain a curve adequate for the extrapolation of E° values before the anomalies at high dilution appear. One way would be to assume at every concentration complete ionization and obtain the E° value in that way, or, as a first approximation, the degree of dissociation may be assumed to be that given by conductivity. The latter method is employed in this paper. It should be noted that no assumption is made that conductivity values give the thermodynamic degree of dissociation, but that they are used solely as a convenient means of plotting values which by extrapolation give the true E°.

Dissociation of Cadmium Chloride. - The values of the degree of dissociation given by Noyes and Falk[1] were plotted against the logarithm of the concentration, the curve being drawn asymptotic to the line $\alpha = 1$. (α = the degree of dissociation.) The data used for this plot, which is not published herewith, are given in Table V.

Dissociation of Zinc Chloride.—The degree of dissociation of zinc chloride was obtained from the equivalent conductance Λ, given in the Landolt and Bornstein Tables, and the equivalent conductance at infinite dilution, ($\Lambda_0 = 112.5$) given by Noyes and Falk (*Loc. cit.*). The degree of dissociation, α, is obtained by taking the ratio Λ/Λ_0. Values of α for various concentrations are also given in Table V.

TABLE V

Dissociation of Cadmium Chloride and Zinc Chloride

$C(CdCl_2)$ mols per 1000 g of H_2O	α	$C(ZnCl_2)$ mols per 1000 g of water	Λ 1/ohms	α
0.0005	0.931	0.00005	110	0.978
0.0010	0.891	0.00010	109	0.970
0.0025	0.803	0.00025	108	0.961
0.0050	0.735	0.0010	107	0.952
..		0.0025	105	0.934
...	.		101	0.898

Calculation of Normal Electrode Potentials.

The data in Table I give, as a mean value for the cell

$$H_2(1\ atm),\ HCl(0.01\ M),\ \underline{AgCl},\ \underline{Ag},\ E = 0.4665 \text{ volt}.$$

We may now calculate E°, which is the electromotive force of this cell when $H^+ (= Cl^-)$ is (hypothetical) molal, using the equation

$$E = E^\circ - (RT/F) ln(Cl^-)(H^+).$$

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[1] THIS JOURNAL, 34, 475 (1912).

In 0.01 M hydrochloric acid solution, the activity of H^+ (and Cl^-) has been found to be 0.0093.[1] Using this value we obtain,

$$0.4665 = E^\circ - 0.05915 \log(0.0093)^2,$$

from which we get

$$H_2, H^+(M), Cl^-(M), \underline{AgCl}, \underline{Ag}, E^\circ = 0.2283 \text{ volt.}^2$$

When two Faradays of electricity are passed through the cell $\underline{M}$; MCl_2, $\underline{AgCl}$; $\underline{Ag}$, the following reaction takes place

$$\underline{M} + 2\underline{AgCl} = M^{++} + 2Cl^- + 2\underline{Ag}$$

The e. m. f. of the cell is given by the following equation:

$$E = E^\circ - (RT/2F)\, ln\, (4C^3\alpha^3),$$
$$= E^\circ - 0.08873 \log (1.588\, C\alpha),$$

in which E° is the potential when M^{++} and Cl^- are each (hypothetical) molal (*i. e.*, E° is the normal potential of the metal M); R is the gas constant; T is the absolute temperature; F is the faraday (= 96500 coulombs), C is the concentration of the chloride solution in mols per 1000 g. of water; and α is the fraction ionized. In using this equation it is assumed that $C\alpha$ is practically equal to the activity of the metal ion. Using this equation by substituting it in observed values of α belonging to the concentrations C, a series of E° values was obtained. The values thus calculated are given in Tables VI and VII for cadmium and zinc, respectively.

TABLE VI

Normal Potential of Cadmium

Log *C* -10	α	*E* volt	E° volt.
6.0000	0.975	0.9597	0.6218
6.1000	0.970	0.9523	0.6231
6.2000	0.966	0.9445	0.6240
6.3000	0.961	0.9365	0.6245
6.4000	0.955	0.9282	0.6250
6.5000	0.948	0.9199	0.6253
6.6000	0.940	0.9117	0.6258
6.7000	0.931	0.9035	0.6259
6.8000	0.919	0.8954	0.6262
6.9000	0.904	0.8876	0.6266
7.0000	0.888	0.8801	0.6272
7.6000	0.758	0.8362	0.6306

The curve of observed electromotive force ought to become steeper as the cadmium chloride becomes more dilute, until complete dissociation has taken place, when the slope of the curve should be 0.0887 volt per unit change in log C. Owing to the large effect of impurities, etc., when the solutions are very dilute, the curve not only becomes straight before the theoretical slope is reached, but actually bends over. Now the true $E°$ curve would continue to fall out to infinite dilution, but the experimental errors at small concentrations cause a rapid fall of the curve, producing a point of inflection. This rapid fall probably has begun to manifest itself even before the point of inflection is reached. It is $E°$ at this point of inflection which is taken as the most probable value of the true $E°$.

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[1] Lewis, Brighton and Sebastian, *Loc. cit.*

[2] From this value of E° might be calculated the free energy of formation of the particular silver chloride used.

The values of $E°$ in *Table VI* were plotted against log C (Fig. 3) and from this plot was obtained the final value, $E° = 0.6255$ volt.

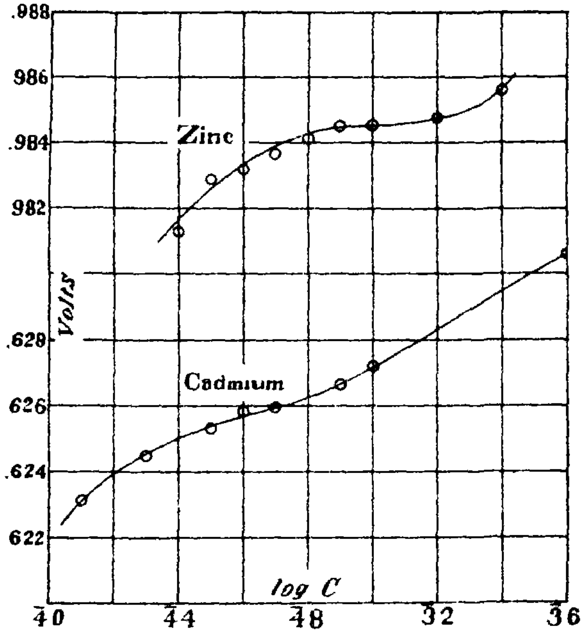

Fig 3

We may write for the cell Cd, $Cd^{++}(M)$.Cl (M) $\underline{AgCl}$: $\underline{Ag}$, $E° = 0.6255$. As we have already calculated, $H_2 \cdot H^{+}(M)$ $Cl^{-}(M)$; $\underline{AgCl}$; $\underline{Ag}$, $E° = 0.2263$. Combining these two, we obtain, $\underline{Cd}$: $Cd^{++}(M) \cdot H^{+}(M)$; H_2; $E° = 0.3992$. Since the normal potential of the hydrogen electrode is taken as zero, the e. m. f. of the above cell gives us directly the normal potential of the cadmium electrode

$$\underline{Cd}: Cd^{++}(M), E° = 0.3992.$$

This value probably is good to 0.0010 volt.

TABLE VII

Normal Potential of Zinc

Log C —10.	α.	E volts	$E°$ volt.
6.4000	0.962	1.2844	0.9813
6.5000	0.958	1.2772	0.9829
6.6000	0.954	1.2688	0.9832
6.7000	0.949	1.2606	0.9836
6.8000	0.944	1.2524	0.9841
6.9000	0.937	1.2442	0.9845
7.0000	0.930	1.2356	0.9845
7.2000	0.910	1.2189	0.9847
7.4000	0.886	1.2032	0.9856

The values of $E°$ for zinc (Table VII) were plotted against log C as in the case of cadmium (see Fig. 3). From this curve we obtain

$$\underline{\mathrm{Zn}};\ \mathrm{Zn}^{++}(M)\ \mathrm{Cl}^-(M)\cdot\underline{\mathrm{AgCl}}\ \underline{\mathrm{Ag}},\ E° = 0.9845$$

As already given, $\mathrm{H}_2\cdot\ \mathrm{H}^+(M)\ \mathrm{Cl}^-(M);\ \underline{\mathrm{AgCl}};\ \underline{\mathrm{Ag}},\ E° = 0.2263$

Combining these two we find $\underline{\mathrm{Zn}}\cdot\mathrm{Zn}^{++}(M),\ \mathrm{H}^+(M)\ \ \mathrm{H}_2,\ E° = 0.7582$.

The e. m. f. of this cell is the normal potential of the zinc electrode

$$\underline{\mathrm{Zn}},\ \mathrm{Zn}^{++}(M),\ E° = 0.758.$$

On account of the uncertainty in the electromotive force measurements in the case of zinc, the above value may have an error as large as 0.002 volt

Free Energy of Dilution.

If we have two cells of the type $\underline{\mathrm{M}},\ \mathrm{MCl}_2,\ \underline{\mathrm{AgCl}},\ \underline{\mathrm{Ag}}$, where the concentration of the MCl_2 solutions are C_1 and C_2, respectively, the difference between the e. m. f. of the two cells multiplied by twice the faraday equivalent and divided by the mechanical equivalent of heat (4.182) gives the free energy of dilution, in calories, of the MCl_2 solution from the concentration C_1 to the concentration C_2. That is,

$$\Delta F = \frac{\Delta E \times 96500}{4.182}.$$

A series of values thus calculated are given in Table VIII.

TABLE VIII

Free Energy of Dilution of Cells.

C_1 M	C_2 M	ΔF (CdCl_2) Calc	ΔF (ZnCl_2) Calc
0.1	0.01	1306	
0.05	0.005	1426	
0.01	0.001	1615	1719
0.005	0.0005	1705	1858
0.002	0.0002	1818	
0.003	0.0003		1888

If the salt were completely dissociated the slope of the electromotive-force curve (Fig. 3) ought to be 0.0887 volt. That is, for a tenfold change in concentration the free energy of dilution ought to approach the value $0.0887 \times 96500/4.182 = 2046$ calories, in the more dilute solutions. That this value is approached more nearly by the zinc chloride than by the cadmium chloride indicates that zinc chloride is dissociated to a higher degree. Conductance ratios also show zinc chloride to be the more highly dissociated.

The author takes this opportunity to acknowledge the helpful suggestions of, and to express his indebtedness to, Dr. Gilbert N. Lewis, in whose laboratory this work was conducted.

Summary.

Previous work by the author, in which mercurous sulfate was used in a reference electrode, is discussed and the reason for the inaccuracy noted. From the electromotive force of the cell $\underline{\mathrm{Zn}}$, $\mathrm{ZnSO_4}$; $\mathrm{Hg_2SO_4}$; Hg, the normal electrode potential of zinc was calculated to be 0.76 volt, with a probable accuracy of only 0.01 volt.

In the present work the e. m. fs. of the following cells have been measured:

$\underline{\mathrm{Zn}}$: $\mathrm{ZnCl_2}$: $\underline{\mathrm{AgCl}}$: $\underline{\mathrm{Ag}}$;
Cd(amalgam): $\mathrm{CdCl_2}$: $\underline{\mathrm{AgCl}}$: $\underline{\mathrm{Ag}}$;
Cd (amalgam): $\mathrm{CdCl_2}$; $\underline{\mathrm{Cd}}$;
$\mathrm{H_2}$; HCl(0.01*M*); $\underline{\mathrm{AgCl}}$: $\underline{\mathrm{Ag}}$

In the first cell the concentrations of the zinc chloride solutions ranged from 0.0003 *M* up to 0.01 *M*. In the second, the concentrations of cadmium chloride ranged from 0.0001 *M* up to saturation (6.61 *M*). All measurements were carried out at a temperature of 25°.

The normal electrode potentials of zinc and cadmium were found to be (zinc) 0.758 ± 0.002 volt and (cadmium) 0.3992 ± 0.0010 volt, the normal potential of the hydrogen electrode being taken equal to zero.

The free energy of dilution of zinc chloride and cadmium chloride solutions was obtained.

Berkeley, Cal

[CONTRIBUTION FROM THE BUREAU OF STANDARDS, U. S. DEPARTMENT OF COMMERCE.]

THE DETERMINATION OF ZIRCONIUM BY THE PHOSPHATE METHOD.

BY G. E. F. LUNDELL AND H. B. KNOWLES.[1]

Received September 7, 1919.

CONTENTS.—I. Introduction. II. General Principles. III Historical IV. Precipitation of Zirconium Phosphate. 1. Permissible Acidity; 2. Excess of Precipitant Required; 3. Effect of Hydrogen Peroxide; 4 Precipitation Temperature. V. Washing the Precipitate. VI. Ignition of the Precipitate. VII. Procedure Recommended. VIII. Confirmatory Experiments IX. Separation from Other Elements: 1. Iron, Aluminum and Chromium; 2. Titanium; 3. Cerium; 4. Thorium. X Summary.

I. Introduction.

The determination of zirconium in ores and metallurgical products has aroused considerable interest during the past year. The method most often proposed has been the phosphate method originally devised by Hillebrand for the determination of the small amounts of zirconium usually found in ordinary rocks. It is the purpose of this paper to point out the danger involved in applying this method to the determination of large amounts of zirconium, and to give the modifications of the method which have been found to increase its accuracy.

II. General Principles.

The phosphate method consists essentially in precipitating zirconium from weak sulfuric acid solution by means of alkali phosphate. If titanium is present, hydrogen peroxide is added to keep it in solution. Water is usually specified by word[2] or by inference[3] as the washing medium, although acid washes have been recommended.[4] The washed precipitate is ignited to constant weight and various factors for its zirconium content have been given: 38.38[1], 36.00[2], 38.28[3]%. The zirconium factor for ZrP_2O_7 is 34.23% while the factor for the compound $5ZrO_2.4P_2O_5$ mentioned by Hillebrand and described in Gmelin-Kraut[5] is 38.35%.

It is evident that the use of any of these factors will not lead to serious errors on precipitates weighing two or three mg. In case of large precipitates the indiscriminate use of these factors cannot but lead to serious errors.

It was in the hope of discovering whether zirconium could be quantitatively separated, from ordinary contaminants, as a precipitate which would yield a residue of definite composition upon ignition, that the following work was undertaken:

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[1] Published by permission of the Director of the Bureau of Standards.

[2] Johnson, *Chem. Met. Eng.*, 20, 588 (1919).

[3] Nicolardot and Reglade, *Compt. rend.*, 168, 349 (1919).

[4] Ferguson, *Eng. Mining J.*, 106, 793 (1918).

[5] Gmelin-Kraut, 1886, p. 703.

III. Historical.

The phosphate method was first used by Hillebrand and described by him in U. S. Geological Survey, *Bulletin* 148 on "The Analysis of Silicate and Carbonate Rocks." The author recommended the method for the determination of the small amounts of zirconium usually found in rocks (from 0.02 to 0.2%), and the following statements were made: "*For the small amounts usually met with it is safe to assume that the* ignited phosphate contains 50% of ZrO_2 (51.8 by theory). If the amount is rather large, it may be safer to fuse with sodium carbonate, leach, ignite, fuse with pyrosulfate, reprecipitate by ammonia, and weigh as ZrO_2." This method has been widely quoted, with the frequent omission, however, of the qualifying sentences given above. As a consequence, several methods for the determination of the larger amounts of zirconium in ores and metallurgical products have recently been published which feature the phosphate method and which specify the use of a zirconium factor based on Hillebrand's recommendation for the ignited phosphate obtained from the very small amounts of zirconium in ordinary rocks.

Steiger[1] in a brief note dealing with some tests of the method draws the following conclusions: 1. Solutions containing at least 3% and perhaps as much as 5% (by weight) of free sulfuric acid may be employed in the phosphate precipitation. 2. The results indicate that basic phosphates are obtained in feebly acid solutions while an increase of acidity tends to give the normal phosphate. 3. Sufficiently accurate results can be obtained in determining the small amounts of zirconium in the average rocks by assuming that the ignited phosphate has the formula ZrP_2O_7 and that it contains 46.32% of ZrO_2. Steiger's data, however, demonstrate conclusively that the composition of the ignited phosphate is extremely variable.

More recently, Nicolardot and Reglade[2] have shown that complete precipitation of zirconium as phosphate may be obtained in a 20% (by weight) sulfuric acid, provided a good excess of the precipitant, ammonium phosphate, be used. They state that for an ignited phosphate obtained from a neutral solution the ZrO_2 factor 0.4870 is indicated. For a 20% acidity, however, their results indicate 0.493 as the ZrO_2 factor.

IV. Precipitation of Zirconium Phosphate.

Factors which must be considered in the precipitation of zirconium as phosphate are (1) permissible acidity; (2) excess of precipitant required; (3) effect of hydrogen peroxide; (4) precipitation temperature. The results of an investigation of the effect of these variables, which was carried on at this Bureau before the publication of the article by Nicolardot and Reglade[1] are summarized below.

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[1] *J. Wash. Acad. Sci.*, 8, 637 (1918).

[2] *Compt. rend., Loc. cit.*

1. **Permissible Acidity.**—Table I gives a summary of the work dealing with the effect of variations in acidity.

TABLE I —EFFECT OF VARIATIONS IN ACIDITY

ZrO_2 Taken 0 0216 g Total volume, 300 cc

Expt	H_2SO_4 (Sp gr 1 84) % by vol	P_2O_5 added × theory (Zr : 2P) G	Ppt obtained G	ZrO_2 found calculated on basis ZrP_2O_7	Error G ZrO_2
1	0 5	10	0 0451	0 0209[2]	—0 0007
2	0 5	10	0 0455	0 0211[2]	—0 0005
3	1 0	10	0 0461	0 0214	—0 0002
4	1 0	10	0 0466	0 0216	—0 0000
5	1 0	100	0 0462	0 0214	—0 0002
6	5 0	10	0 0463	0 0214	—0 0002
7	5 0	10	0 0460	0 0213	—0 0003
8	5 0	100	0 0460	0 0213	—0 0003
9	10 0	10	0 0439	0 0203	—0 0013
10	10 0	10	0 0442	0 0205	—0 0011

The data show that with moderate excess of the precipitant (10 times the theoretical requirement), 5% of sulfuric acid by volume is the maximum allowable excess acid in a cold precipitation This bears out the prediction of Steiger[1] Nicolardot and Reglade[1] working with tepid solutions and a much greater excess of the precipitant found that precipitation was complete in a solution containing 20% by weight of sulfuric acid. This observation has been confirmed at this Bureau

The data also indicate that with acidities of 0 5% and lower, basic zirconium phosphates are formed, an observation which was also made by Steiger.

2. **Excess Precipitant Required.**—Table II gives the data obtained by carrying out the precipitations with various amounts of the precipitant

TABLE II —EFFECT OF VARIOUS AMOUNTS OF PRECIPITANT

ZrO_2 Taken 0 0216 g Total Volume, 300 cc

Expt	H_2SO_4 (Sp gr 1 84) % by vol	P_2O_5 added × theory (Zr : 2P) G	Ppt obtained G	ZrO_2 found calculated on basis ZrP_2O_7	Error G ZrO_2
1	1	2	0 0379	0 0176	—0 0040
2	1	5	0 0453	0 0210	—0 0006
3	1	10	0 0461	0 0214	—0 0002
4	1	100	0 0462	0 0214	—0 0002
5	5	2	0 0380	0 0176	—0 0040
6	5	5	0 0413	0 0191	—0 0025
7	5	10	0 0463	0 0214	—0 0002
8	5	100	0 0460	0 0213	—0 0003

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[1] *Loc. cit*

[2] Qualitative test showed complete precipitation of zirconium.

The above experiments show that a precipitate of normal composition cannot be obtained unless a fair excess of soluble phosphate is used, the excess varying directly with the acid concentration. Nicolardot and Reglade succeeded in getting complete precipitation in an acidity as high as 20% sulfuric by weight by using a very large excess of the precipitant.

3. **Effect of Hydrogen Peroxide.**—Since Hillebrand's method calls for the use of hydrogen peroxide when titanium is present, the tests given in Table III were carried out to determine whether peroxide disturbed the reaction.

TABLE III.—EFFECT OF HYDROGEN PEROXIDE.

ZrO_2 Taken, 0.0216 g. Total Volume, 300 cc.

Expt.	H_2SO_4 (Sp. gr. 1.84) % by vol.	P_2O_5 added × theory (Zr 2P)	3% H_2O_2 Cc	Ppt obtained G	ZrO_2 found calculated on basis of ZrP_2O_7	Error G. ZrO_2
1	1.0	10	10	0.0462	0.0214	−0.0002
2	1.0	100	10	0.0463	0.0214	−0.0002
3	5.0	10	10	0.0460	0.0213	−0.0003
4	5.0	100	10	0.0465	0.0216	−0.0000
5	11.5	100	None[1]	0.0458	0.0212	−0.0004

The experiments show that hydrogen peroxide has no disturbing effect on the phosphate precipitation. The last test was carried out to establish whether excessive amounts of acetanilide which might be introduced with peroxide would disturb the precipitation.

4. **Precipitation Temperature.**—Table IV gives data obtained in phosphate precipitations which were carried on at room temperatures and by digestion on the steam bath followed by filtration of the hot solutions.

TABLE IV.—EFFECT OF TEMPERATURE

ZrO_2 Taken, 0.0216 g. Total Volume, 300 cc. P_2O_5 added, 10 × Theory (Zr 2P).

Expt.	H_2SO_4 (Sp. gr. 1.84) % by vol.	Temp. of precipitation and filtration.	Ppt obtained G	ZrO_2 found calculated on basis ZrP_2O_7	Error G ZrO_2
1	1	Cold	0.0461	0.0214	−0.0002
2	1	Hot	0.0451	0.0209	−0.0007
3	5	Cold	0.0463	0.0214	−0.0002
4	5	Hot	0.0434	0.0201	−0.0015
5	10	Cold	0.0439	0.0203	−0.0013
6	10	Hot	0.0410	0.0190	−0.0026

The data demonstrate that the solubility of zirconium phosphate increases markedly in hot acid solutions. Undoubtedly the solubility in hot solutions could be decreased by adding a larger excess of the precipitant. At the time these experiments were performed no particular advantage resulting from the use of hot solutions was anticipated; consequently the tests were not pursued further. Nicolardot and Reglade, however, have demonstrated that precipitation is complete in luke warm or tepid solutions of high acidity, provided adequate phosphate is used.

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[1] 0.0059 g. acetanilide added; total volume here 100 cc.

The experiments which are given in Tables I, II, III and IV demonstrate that complete precipitation of zirconium as phosphate of definite composition may be had in cold or tepid solution containing: (1) hydrogen peroxide, (2) sulfuric acid ranging from 2 to 20% by weight and (3) secondary ammonium phosphate in 10 to 100 times the theoretical requirement.

V. Washing the Precipitate.

Since water is the washing medium usually employed in the phosphate determination, qualitative tests were carried out to determine whether zirconium phosphate is soluble in water or whether it suffers hydrolysis during the washing operation. It was found that no zirconium whatever could be obtained by treating with ammonium hydroxide the water washings of zirconium phosphate precipitates. It was found, however, that very considerable amounts of phosphoric acid were present in wash waters obtained by washing with water, zirconium phosphate precipitates which had first been thoroughly washed with 5% ammonium nitrate. This observation was verified quantitatively and in Table V are shown the differences noted between determinations which were varied only in washing treatment.

TABLE V.—EFFECT OF WASHING TREATMENT

Total Weight of Solution, 100 g Total Volume Wash Soln., 300 cc ZrO_2 Taken, 0.0216 g H_2SO_4, 20% by Weight P_2O_5 added, 100 × Theory (Zr : 2P).

Expt	Wash solution used	Ppt obtained G	ZrO_2 found calculated on basis ZrP_2O_7	Error G ZrO_2.
1....	H_2O	0.0438[1]	0.0203	—0.0013
2.....	H_2O	0.0445[1]	0.0206	—0.0010
3.....	NH_4NO_3 5%	0.0458[2]	0.0212	—0.0004
4......	NH_4NO_3 5%	0.0461[2]	0.0214	—0.0002

The data in Table V demonstrate that no definite composition can be ascribed to an ignited water-washed phosphate and that use of a cold 5% ammonium nitrate solution almost entirely overcomes the tendency toward hydrolysis.

VI. Ignition of Precipitate.

No special precautions were given by Hillebrand for the ignition of the phosphate precipitate and none are necessary for the small amounts encountered in ordinary rock analysis. It was soon found, however, at this Bureau that the ignition of zirconium phosphate precipitates weighing approximately 0.02 g. was a hard problem because of difficulty in burning off carbon and the marked tendency of the precipitate to decrepitate.

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[1] Washings gave negative tests for zirconium but heavy tests for P_2O_5.

[2] Washings gave negative tests for zirconium and *very faint* tests for P_2O_5.

Nicolardot and Reglade call attention to the decrepitation of the phosphate and they also state that the final ignited product is gray-white. A water-washed precipitate such as they obtained does exhibit a strong tendency to decrepitate and it is also difficult to burn white. In fact, we have sometimes obtained from water-washed precipitates black residues of excessive weight which resisted all ignition treatments, including ignition in oxygen. The use of a properly prepared Gooch crucible obviated all these troubles but was not adopted as a standard procedure since it does not permit of convenient examination of the final weighed product. The ammonium nitrate wash which was finally adopted leaves the paper and the precipitate in the most desirable condition for the ignition, and a pure white phosphate can be obtained provided the preliminary ignition is carried on at a low temperature. Decrepitation difficulties are less marked, but with precipitates weighing more than 0.005 g. ignitions should be cautiously carried on with crucibles partly covered, particularly at the stage when the carbon envelope is burning away. The final ignition should be done over the blast lamp or Méker burner for 15 minutes. Zirconium pyrophosphate is not hygroscopic as is shown in Table VI.

TABLE VI.—EXPOSURE OF IGNITED PYROPHOSPHATE

	Wt of ZrP_2O_7	
Expt	After ignition	After 4 hours' exposure to atmosphere
1	0.0920	0.0919
2	0.0463	0.0463

VII. Procedure Recommended.

The procedure following is a modification of that published by Nicolardot and Reglade.

A. Volume of Solution.—From 25 cc. for small amounts (0.0005 g. ZrO_2) to 200 cc. for larger amounts (0.1 g.).

B. Acidity.—20% sulfuric acid by weight.

C. Hydrogen Peroxide.—Sufficient to keep titanium dioxide peroxidized; 10 cc. will do no harm.

D. Precipitant.—Secondary ammonium phosphate in excess. From 10 to 100 times the theoretical requirement as expressed by the ratio $Zr:P_2O_5$ should be used. The larger excess is desirable when small amounts of zirconium dioxide are to be determined.

E. Precipitation conditions.

1. Temperature. Cold or 40–50°, preferably the latter.
2. Time. Two hours for amounts of zirconium dioxide in excess of 0.005 g. Six hours or longer for smaller amounts.

F. Filtration.—Warm; decant as much supernatant liquid as possible to avoid clogging the filter.

G. Washing.—With cold 5% ammonium nitrate solution

H. Ignition.—Very careful ignition in a partially covered platinum crucible over a low flame until the filter paper carbon is destroyed, followed by blasting or its equivalent

VIII. Confirmatory Experiments.

The results given in Table VII which were obtained by the procedure recommended, demonstrate that the method is reasonably accurate

TABLE VII—RESULTS WITH RECOMMENDED PROCEDURE

H_2SO_4, 20% by Weight, Total Volume of Solution, 100 cc $(NH_4)_2HPO_4$ Taken, 1 0 g, Wash Solution, 5% NH_4NO_3

Expt	H_2O_2 Cc	TiO_2 added G	Zr phosphate weighed G	ZrO_2 found calculated on basis ZrP_2O_7 G	ZrO_2 added G	Diff G ZrO_2
1	10	none	0 0014	0 00065	0 00064	+0 00001
2	10	none	0 0023	0 00106	0 00107	—0 00001
3	10	none	0 0040	0 00185	0 00193	—0 00008
4	10	0 0990	0 0022	0 00102	0 00107	—0 00005
5	none	none	0 0453[1]	0 0210	0 0216	—0 0006
6	none	none	0 0458	0 0212	0 0216	—0 0004
7	10	none	0 0461	0 0214	0 0216	—0 0002
8	10	none	0 0457	0 0212	0 0216	—0 0004
9	none	none	0 0458	0 0212	0 0216	—0 0004
10	none	none	0 0920[1]	0 0426	0 0431	—0 0005

It will be noticed that the values obtained are slightly lower than theoretical amounts This was expected on account of the slight hydrolysis during the washing of the precipitate and the difficulty in preventing losses due to decrepitation.

IX. Separation from Other Elements.

1. Iron, Aluminum and Chromium—Nicolardot and Reglade have shown that a perfect separation from aluminum, chromium and iron can be had by the procedure outlined.

2. Titanium.—Before the publication of the paper of Nicolardot and Reglade, tests made at this Bureau demonstrated that complete separation from titanium was possible by one precipitation in the presence of hydrogen peroxide in solutions of lower acidity than 20% by weight. A summary of the results obtained is given in Table VIII.

TABLE VIII - SEPARATION FROM TITANIUM

Expt No	TiO_2 added G	ZrO_2 added G	H_2SO_4 present	ZrP_2O_7 obtained G	ZrO_2 equivalent G	Error G ZrO_2	Results of colorimeter tests of ignited residues
1 .	0 0990	0 00107	20% by wt	0 0022	0 00102	—0 00005	Ti-faint trace[2]
2 ..	0 0198	0 0216	1% by vol	0 0461	0 0214	—0 0002	Ti-faint trace[2]
3	0 0198	0 0216	5% by vol	0 0464	0 0215	—0 0001	Ti-faint trace[2]

[1] Decrepitation

[2] Less than 0 00005 g. of TiO_2.

3. Cerium.—The data given in Table IX show that zirconium can be quantitatively separated from cerium present in either of its valences.

TABLE IX.—SEPARATION FROM CERIUM.

Expt.	ZrO_2 added G	Cerium oxide added G	H_2O_2 Cc	ZrP_2O_7 found	ZrO_2 calculated on basis ZrP_2O_7	Error G ZrO_2
1........	0 0216	0 0246 Ce_2O_3	none	0 0457	0.0212	—0.0004
2........	0 0216	0 0246 Ce_2O_3	10	0 0453	0 0210	—0.0006
3........	0 0216	0 0246 CeO_2	none	0 0449	0 0208	—0 0008

4. Thorium.—The data given in Table X show that zirconium can be quantitatively separated from thorium by the method given.

TABLE X—SEPARATION FROM THORIUM

Expt	ZrO_2 added G	ThO_2 added G	H_2SO_4 (Sp gr 1 84) Cc	H_2O_2 Cc	$(NH_4)_2HPO_4$ G	ZrP_2O_7 found	ZrO_2 calculated on basis ZrP_2O_7	Error G ZrO_2
1.....	0 0216	0 0263	11 5	none	1	0 0470	0 0218	+0 0002
2....	0 0216	0 0263	11 5	10	1	0 0465	0 0215	—0 0001

X. Summary.

From the above experiments made at the Bureau of Standards and elsewhere, the following conclusions may be drawn:

1. Zirconium can be quantitatively precipitated as secondary zirconium phosphate in cold or tepid solutions containing from 2 to 20% by weight of sulfuric acid, provided a 10–100-fold excess of the precipitant diammonium phosphate, is used.

2. Hydrolysis, which occurs when the phosphate precipitate is washed with water, can be almost entirely avoided by the use of a cold 5% ammonium nitrate washing solution.

3. Zirconium pyrophosphate, for which the ZrO_2 factor is 0.4632, is obtained upon ignition of a secondary zirconium phosphate which had been washed with ammonium nitrate solution.

4. No definite composition can be ascribed to a compound resulting upon ignition of a secondary zirconium phosphate which has been washed with water.

5. Zirconium can be quantitatively separated as phosphate in a 20% by weight sulfuric acid solution from iron, aluminum, chromium, cerium and thorium. The separation from titanium is satisfactory provided hydrogen peroxide is present.

WASHINGTON, D C

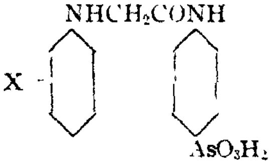
[CONTRIBUTION FROM THE LABORATORIES OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH.]

AROMATIC ARSENIC COMPOUNDS. V. *N*-SUBSTITUTED GLYCYLARSANILIC ACIDS.

BY WALTER A. JACOBS AND MICHAEL HEIDELBERGER

Received July 2, 1919

The substances discussed in the present communication are closely related to the previously described substituted anilides of phenylglycine-*p*-arsonic acid,[1] but differ from these in the fact that the glycine side chain is reversed, the arsonic acid radical becoming a substituent on the anilide nucleus, as follows:



These substances were readily prepared by boiling the sodium salt of chloroacetylarsanilic acid with the aromatic amino compound, the condensation occurring in boiling aqueous solution within 15 to 30 minutes, owing to the reactivity of the chlorine in the former substance. The first member of the series, glycylarsanilic acid, was prepared by the use of ammonia in this reaction and was accompanied by the formation of the secondary imino compound. With the aromatic amines no difficulty was experienced in any case and the reaction has proved capable of wide extension. We have confined our studies up to the present to those compounds which were prepared for biological investigation.

The fundamental compound required in this work was chloroacetylarsanilic acid. This derivative has already been mentioned in German patent 191,548, but as far as we could ascertain it has not been employed for the synthesis of other arsenic compounds. The patent contains a method for its preparation by the interaction of arsanilic acid and chloroacetyl chloride, but we have found it unsuitable for the preparation of the substance in large quantities as the reaction was difficult to control and the yields were poor and uncertain. A very serviceable and simple means was found for the large scale preparation of chloroacetyl-arsanilic acid, consisting in heating arsanilic acid with an excess of chloroacetic acid on the water bath, an excellent yield of the pure substance being easily obtained.

The substituted phenylglycyl-arsanilic acids resemble in general properties the isomeric anilides of phenylglycine-*p*-arsonic acid, functioning both as acids and feeble bases. They are but sparingly soluble in the usual solvents and all have high melting or decomposition points, the observed values depending upon the rate of heating. In general, the sodium salts were readily soluble in water.

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[1] THIS JOURNAL, 41, 1610 (1919).

Experimental.

Chloroacetyl-arsanilic Acid, *p*-$H_2O_3AsC_6H_4NHCOCH_2Cl$.—A method for the preparation of chloroacetyl-arsanilic acid has been given in German patent 191,548. In addition to the fact that no full description of the substance is given, we have found the following method more serviceable for its preparation in large quantity: 50 g. of arsanilic acid and 150 g. of dry chloroacetic acid are heated in an open flask on the water bath for 2 hours. The mixture gradually forms a clear melt, and towards the end the chloroacetyl-arsanilic acid occasionally begins to separate. The melt is poured into about a liter of well stirred, saturated sodium chloride solution, and the precipitated arsonic acid is filtered off and washed well with water. Yield, 50 g. A portion of the acid was dissolved in hot water, treated with bone black, and the filtered solution cooled rapidly in order to prevent decomposition. Under these conditions it separates as minute, lenticular platelets and toothed leaflets which contain no water of crystallization and which darken when rapidly heated, but melt and decompose only when the temperature of the bath is held at 285° for a few moments. The acid is readily soluble in hot alcohol, somewhat less so in boiling water or acetic acid, and sparingly soluble in the last two in the cold and in acetone. It is slowly acted upon by prolonged exposure to moist air.

Subst., 0.1867 (Kjeldahl), 6.25 cc. 0.1 *N* HCl. Subst., 0.1342 (Carius), AgCl, 0.0634.

Subst., 0.2824; $Mg_2As_2O_7$, 0.1481.

Calc. for $C_8H_9O_4NClAs$: N, 4.77; Cl, 12.08; As, 25.53. Found: N, 4.69; Cl, 11.69; As, 25.31.

Practically as good an analysis was obtained on the crude product, and this was used in all of the following preparations:

Glycyl-*p*-arsanilic Acid, *p*-$H_2NCH_2CONHC_6H_4AsO_3H_2$.—20 g. of chloroacetyl-arsanilic acid were added to 100 cc. of conc. aqueous ammonia, warmed gently to about 30° until solution was complete, and allowed to stand overnight. The excess of ammonia was then boiled off from the clear solution, causing the crude reaction product to crystallize. After cooling this was filtered off, 12 g. being obtained. The product was purified by treating with dil. hydrochloric acid, avoiding a large excess on account of the consequent precipitation of the hydrochloride of the glycine. After filtering off the imino compound (see below) the crude glycylaminophenyl-arsonic acid was precipitated by adding sodium acetate. For further purification it was dissolved in just enough dil. sodium hydroxide solution and then precipitated by means of a stream of carbon dioxide. A repetition of the final purification was necessary before good analytical figures could be obtained, a considerable loss of material also taking place. The pure amino acid forms minute, toothed, glistening plates which are anhydrous, do not melt below 295°, and are very difficultly soluble in boiling water or 50% alcohol It functions as a very weak acid, being soluble only in an excess of weak bases, such as ammonia, and is displaced from its salts by carbon dioxide

Subs, 0 1328, 11 8 cc N (24 5°, 751 mm) Subs, 0 3101, $Mg_2As_2O_7$, 0 1743
Calc for $C_8H_{11}O_4N_2As$ N, 10 22, As, 27 34 Found N, 10 08, As, 27 12

Iminobisacetyl-*p*-arsanilic Acid, $(p\text{-}H_2O_3AsC_6H_4NHCOCH_2)_2NH$ — The hydrochloric acid-insoluble fraction obtained in the preparation of the *p*-glycylarsanilic acid was dissolved in dil. sodium hydroxide solution, precipitated with an excess of hydrochloric acid, further purified by a repetition of this process, and finally recrystallized by dissolving in hot, dil ammonium hydroxide and adding acetic acid in excess. The imino acid separated as glistening rosets of microcrystals Before filtering, the solution was cooled and acidified to congo red with hydrochloric acid. The substance darkens at 280–5° without melting, and is practically insoluble in the usual solvents

Subs, 0 1318, 9 2 cc N (29 0°, 757 mm) Subs 0 3401, Mg_2As_2O, 0 1987
Calc for $C_{16}H_{19}O_8N_3As_2$ N, 7 92, As, 28 23 Found N, 7 86, As, 28 19

***N*-Methylglycyl-*p*-arsanilic Acid,** *p* $CH_3NHCH_2CONHC_6H_4AsO_3H_2$ A strong methylamine solution was prepared by treating 25 g. of methylamine hydrochloride with 60 g of well chilled, 25% sodium hydroxide solution Without removing the precipitated sodium chloride, 5 g. of chloroacetylarsanilic acid were added. On allowing to warm to room temperature and breaking up the lumps with a rod, the acid soon dissolved After 24 hours' standing the excess of methylamine was removed on the water bath and on diluting the residue and acidifying strongly with acetic acid the arsonic acid slowly crystallized. Recrystallized from water it separates as long, silky, glistening needles which contain approximately two molecules of water of crystallization. The yield was 2 g. It turns brown at about 250° but does not melt below 275°. It is practically insoluble in hot alcohol and is not very freely soluble in boiling water It dissolves in dilute mineral acids and on adding sodium nitrite to the solution in dil hydrochloric acid the nitroso derivative deposits on rubbing as sheaves and spheres of microscopic needles.

Subs, air-dry, 0 5641, loss, 0 0670 *in vacuo* at 100° over H_2SO_4.
Calc for $C_9H_{13}O_4N_2As \cdot 2H_2O$ H_2O, 11 12 Found· 11 87
Subs, anhydrous, 0 1864 (Kjeldahl), 12 85 cc 0 1 *N* HCl Subs, 0 2635, $Mg_2As_2O_7$, 0 1404
Calc for $C_9H_{13}O_4N_2As$ N, 9 73, As, 26 00 Found· N, 9 66, As, 25 72

***N*-Phenylglycyl-*p*-arsanilic Acid (*N*-Phenylglycineanilide-*p*′-arsonic Acid),** $p\text{-}C_6H_5NHCH_2CONHC_6H_4AsO_3H_2$.—This substance, isomeric with phenylglycineanilide-*p*-arsonic acid,[1] was prepared as follows: 2 g. of aniline in 15 cc. of alcohol were added to a solution of 4.5 g. of chloroacetyl-arsanilic acid in 15 cc. of *N* sodium hydroxide solution. The solution was boiled for 1/2 hour under an air-condenser, finally setting to a crystalline cake. The yield of acid was 4.4 g. Recrystallized from 50% alcohol the arsonic acid forms delicate, felted needles which are almost insoluble in boiling water. When heated it darkens slightly, but does not melt below 280°. When a suspension of the acid in hot 50% acetic acid is treated with excess sodium nitrite it dissolves at once, the nitroso compound soon crystallizing from the solution as nacreous plates.

Subs., 0.3260; (Kjeldahl) 18.70 cc 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1435.

Calc for $C_{14}H_{15}O_4N_2As$ N, 8.00; As, 21.39 Found N, 8.04; As, 21.24.

***m*-Oxaminophenyl-glycyl-*p*-arsanilic Acid,** *m*-$HO_2CCONHC_6H_4NH$-$CH_2CONHC_6H_4AsO_3H_2(p')$.—12 g. of chloroacetyl-arsanilic acid and 7.2 g. of *m*-amino-oxanilic acid[2] were dissolved in 80 cc. of *N* sodium hydroxide solution and boiled for 20 minutes. The small amount of crystalline material which separated on cooling was filtered off and the filtrate made acid to congo red. A dark-colored gum separated, but the supernatant liquid, on standing overnight, deposited a crystalline crust. This was dissolved in very dilute aqueous ammonia and hydrochloric acid added to the solution until a faint turbidity persisted. This contained much coloring matter and was filtered off. It was found that if hydrochloric acid was added directly to the filtrate only a caseous precipitate could be obtained, but if acetic acid was first added in sufficient amount and then hydrochloric acid until definitely blue to congo red paper, the solution, when seeded, deposited the *hydrochloride* of the oxamino acid as aggregates of microscopic plumes, which gradually lost hydrochloric acid on standing in moist air.

Subs., 0.1546; 12.0 cc N (17.5°, 750 mm.). Calc. for $C_{16}H_{16}O_7N_3As.HCl$: N, 8.88. Found: 9.00.

A portion of the hydrochloride was boiled with water, causing a change in physical appearance and the elimination of hydrochloric acid. The free *oxamino acid* was filtered off, washed well with hot water, and air-dried, one molecule of water of crystallization being retained. The substance is practically insoluble in boiling water and very sparingly so in 50% alcohol. When rapidly heated to 175°, then slowly, the anhydrous acid effervesces at 179°, with preliminary softening and darkening.

Subs., air-dry, 0.5870; loss 0.0249, at 100° *in vacuo* over H_2SO_4.

Calc. for $C_{16}H_{16}O_7N_3As.H_2O$: H_2O, 3.96. Found: H_2O, 4.24.

Subs., anhydrous, 0.1412; 11.85 cc. N (23.5°, 757 mm.). Subs., 0.3966; $Mg_2As_2O_7$, 0.1389.

Calc. for $C_{16}H_{16}O_7N_3As$: N, 9.61; As, 17.13. Found: N, 9.62; As, 16.90.

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[1] THIS JOURNAL, 41, 1613 (1919).

[2] *Ibid.*, 39, 1451 (1917).

p-Aminophenyl-glycyl-p-arsanilic Acid, $p\text{-}H_2NC_6H_4NHCH_2CONHC_6H_4AsO_3H_2$.—8 g. of *p*-acetamino-phenylglycineanilide-*p'*-arsonic acid (see below) were boiled with 8 parts of 1 : 1 hydrochloric acid for 6 minutes, cooled rapidly, shaken with bone black, filtered, and treated with saturated sodium acetate solution until the disappearance of the congo red reaction. The precipitate was filtered off, dissolved in dil. hydrochloric acid, and the solution filtered and treated again with sodium acetate. The amino acid separated as microcrystalline aggregates which tended to become colloidal on washing with water. The yield was 4.5 g. When rapidly heated the acid darkens and sinters, but does not melt below 280°. It is soluble in dilute mineral acids and alkalies and is practically insoluble in boiling water and very sparingly so in boiling 50% alcohol. It is readily diazotized, giving a red color with R-salt.

Subs., 0.1425; 14.15 cc. N (21.5°, 751 mm.). Subs., 0.3254; $Mg_2As_2O_7$, 0.1367.
Calc. for $C_{14}H_{16}O_4N_3As$ N, 11.51; As, 20.52. Found: N, 11.38: As, 20.27.

p-Acetaminophenyl-glycyl-p-arsanilic Acid.—Starting with 6 g. of *p*-aminoacetanilide, the reaction product began to separate after a few minutes, the heating being continued for one hour on the water bath. The yield of crude acid was 12 g. This was converted into the *sodium salt* by dissolving in warm, dil. sodium hydroxide solution, and salting out the neutral solution with saturated sodium acetate solution. Recrystallized from water containing a small amount of sodium carbonate to prevent hydrolysis to the free acid, it separated as flat, glistening needles which contain 7 molecules of water of crystallization when air-dry. It may also be precipitated from its aqueous solution by the addition of alcohol.

Subs., air-dry, 0.4734; loss 0.1057 at 100° *in vacuo* over H_2SO_4.
Calc. for $7H_2O$: H_2O, 22.72. Found: 22.32.
Subs., anhydrous, 0.2998; (Kjeldahl) 20.50 cc. 0.1 *N* HCl. Subs., 0.3346; $Mg_2As_2O_7$, 0.1193.
Calc. for $C_{16}H_{17}O_5N_3AsNa$: N, 9.79; As, 17.45. Found: N, 9.58; As, 17.22.

On treating a hot dilute solution of the sodium salt with acetic acid, the free *arsonic acid* separated slowly as glistening, hexagonal platelets. It does not melt below 275° and is very sparingly soluble in boiling water or 50% alcohol.

Subs., 0.2117; (Kjeldahl) 15.4 cc. 0.1 *N* HCl.
Calc. for $C_{16}H_{18}O_5N_3As$: N, 10.32. Found: 10.19.

p-Oxaminophenyl-glycyl-p-arsanilic Acid.—14 g. of chloroacetyl-arsanilic acid and 8.4 g. of *p*-amino-oxanilic acid[1] were boiled with 94 cc. of *N* sodium hydroxide solution for 1/2 hour, the product separating after about 10 minutes. The yield was 16.5 g. Reprecipitated from very dilute, hot ammoniacal solution with acetic acid, the arsonic acid separates as slightly

[1] This Journal, 39, 1459 (1917).

purplish aggregates of microscopic crystals containing 1.5 molecules of water of crystallization. It is almost insoluble in boiling water, very sparingly so in boiling 50% alcohol, and, when anhydrous, darkens above 200°, but does not melt below 275°. On heating with aqueous alkali in attempts to hydrolyze the oxamino group the principal products recovered were either the unchanged oxamino compound or arsanilic acid, depending on the length of heating and the strength of alkali. Heating, however, with 1 : 1 hydrochloric acid yielded the amino compound.

Subs., air-dry, 0.4539, loss, 0.0281 *in vacuo* at 100° over H_2SO_4
Calc for $C_{16}H_{16}O_7N_3As \ 1.5H_2O$, H_2O, 5.82 Found: 6.19
Subs., anhydrous, 0.1441, 12.2 cc N (24.0°, 754 mm). Subs., 0.4027, $Mg_2As_2O_7$, 0.1418
Calc. for $C_{16}H_{16}O_7N_3As$ N, 9.61, As, 17.13 Found: N, 9.65; As, 16.99

***p*-Oxamylaminophenyl-glycyl-*p*-arsanilic Acid,** *p*-$H_2NCOCONHC_6H_4$-$NHCH_2CONHC_6H_4AsO_3H_2$.—21 g. of chloroacetyl-arsanilic acid were dissolved in 70 cc of *N* sodium hydroxide solution and added to a boiling solution of 12.6 g. of *p*-amino-oxanilamide[1] in about 300 cc of water. On continuing the boiling the product separated as a partly gelatinous mass which gradually crystallized. After 1/2 hour the hot solution was filtered and the precipitate washed with hot water. It was then suspended in a large volume of hot water and treated with sodium carbonate solution until only a small, gelatinous residue remained. The mixture was treated with bone black and filtered through a hot-water funnel in order to prevent deposition of the sodium salt on the filter. The filtrate was warmed and treated with sodium acetate until crystallization of the salt commenced and was then let stand in the refrigerator. On treating a very dilute, hot solution of the salt with acetic acid, the free arsonic acid separated as clusters of microscopic needles in a yield of 6.5 g. It is practically insoluble in boiling water or 50% alcohol, and does not melt below 285°

Subs., 0.1299, 14.65 cc N (24.0°, 763 mm) Subs., 0.2065, $Mg_2As_2O_7$, 0.0723
Calc for $C_{16}H_{17}O_6N_4As$ N, 12.85, As, 17.19 Found. N, 13.02, As, 16.90.

***p*-Uraminophenyl-glycyl-*p*-arsanilic Acid,** *p*-$H_2NCONHC_6H_4NHCH_2$-$CONHC_6H_4AsO_3H_2$.—12 g. of chloroacetyl-arsanilic acid, 6.1 g. of *p*-aminophenylurea,[2] 40 cc of *N* sodium hydroxide solution, and 20 cc. of saturated sodium acetate solution were boiled for 1/2 hour. On cooling a small amount of precipitate was filtered off and the solution then saturated with sodium acetate and let stand in the ice-box. After 24 hours the precipitate of sodium salt was filtered off, washed with 85% alcohol, dissolved in warm water, treated with bone black, filtered, and the acid precipitated from the filtrate by means of acetic acid. The yield was 7 g. The uramino acid separates as spherular masses of microscopic leaflets which dissolve in boiling 50% alcohol and very sparingly in water. When rapidly heated it changes color above 150° and darkens markedly at about 210°, but does not melt below 285°.

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[1] THIS JOURNAL, 39, 1461 (1917)

[2] *Ibid.*, 39, 1456 (1917)

Subs., 0.1471; 17.7 cc. N (26.0°, 762 mm.). Subs., 0.1858; $Mg_2As_2O_7$, 0.0696.

Calc. for $C_{14}H_{17}O_6N_4As$: N, 13 72, As, 18 35. Found: N, 13.78; As, 18.08.

***m*-Hydroxyphenyl-glycyl-*p*-arsanilic Acid,** *m*-$HOC_6H_4NHCH_2CONHC_6H_4AsO_3H_2$.—Since the oily reaction product from 11 g. of *m*-aminophenol was difficult to obtain in crystalline form, purification was effected by conversion into the *hydrochloride* by adding 100 cc. of 1 : 1 hydrochloric acid to the reaction mixture. The salt was filtered off and washed with 10% hydrochloric acid. A portion, recrystallized from 10% hydrochloric acid, separated as slightly purplish microcrystals which blacken above 140° but do not melt up to 280°. The hydrochloride loses most of its halogen on boiling with water.

Subs., 0.2152 (Kjeldahl), 10.6 cc 0 1 *N* HCl.

Calc. for $C_{14}H_{15}O_5N_2As$ HCl N, 6 96 Found: 6 90

The main portion of this salt was suspended in water and dissolved by the addition of sodium hydroxide solution. On acidifying with hydrochloric acid until just faintly acid to congo red a considerable amount of gummy material was precipitated and was collected with bone black and quickly filtered off. The clear, almost colorless filtrate deposited the crystalline *arsonic acid* on scratching. It was purified by again dissolving in dil. sodium hydroxide solution and acidifying with an excess of acetic acid. The pure arsonic acid separated as pale pink, wedge-shaped, microscopic prisms which contained 3 5 molecules of water of crystallization after air drying. The yield was 15 5 g. On rapid heating the arsonic acid melts at about 80° in its water of crystallization, but rapidly resolidifies. On further heating it turns purple at about 180° and then gradually softens and chars as the temperature is raised. It is easily soluble in ethyl or methyl alcohol or acetone. It dissolves less readily in glacial acetic acid and then separates on scratching in a different form, presumably owing to dehydration. Dilution with water redissolves the crystals. It dissolves readily in boiling water and separates on cooling as a caseous mass.

Subs., air-dry, 0.6257; loss, 0.0893 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{14}H_{15}O_5N_2As.3.5H_2O$: H_2O, 14.68. Found. 14.27.

Subs., anhydrous, 0.1682; (Kjeldahl) 9.35 cc. 0 01 *N* HCl. Subs., 0.2541; $Mg_2As_2O_7$, 0.1064.

Calc. for $C_{14}H_{15}O_5N_2As$: N, 7.66; As, 20.48 Found. N, 7.78; As, 20.21.

***p*-Hydroxyphenyl-glycyl-*p*-arsanilic Acid.**—(From 4.5 g. of *p*-aminophenol.) After a few minutes the reaction product separated from the clear solution and the mixture was then transferred to the water bath and heated one hour. For purification the precipitate was dissolved by neutralization of an aqueous suspension with sodium hydroxide, and the filtered solution treated with 1 : 1 hydrochloric acid until the precipitate which first formed had redissolved. The copious precipitate of the hydrochloride of the arsonic acid which separated on scratching was filtered off. Yield, 11 g. On dissolving in a small volume of dil. sodium hydroxide solution and exactly neutralizing with acetic acid, the *sodium salt* separated on standing in the ice-box. Recrystallized from a small volume of water, it forms aggregates of microscopic needles which contain one molecule of water of crystallization and dissolve sparingly in water at 0° and readily on warming. The aqueous solution of the salt gives a slowly developing pale lilac color with ferric chloride.

Subs., air-dry, 0.3783; loss, 0.0143 at 100° *in vacuo* over H_2SO_4.
Calc. for $C_{14}H_{14}O_6N_2AsNa.H_2O$ H_2O, 4.43. Found: 3.78.
Subs., anhydrous, 0.2833; (Kjeldahl) 14.0 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1134.
Calc. for $C_{14}H_{14}O_6N_2AsNa$ N, 7.22, As, 19.30. Found. N, 6.92; As, 19.32.

On acidifying a hot solution of the salt with acetic acid the free *arsonic acid* separates as aggregates of microscopic hairs which contain approximately one molecule of water of crystallization. The substance is almost insoluble in boiling water or 50% alcohol, and, when anhydrous, blackens and sinters above 200°, but does not melt entirely below 280°.

Subs., air-dry, 0.4903, loss, 0.0265 at 100° *in vacuo* over H_2SO_4
Calc. for $C_{14}H_{15}O_6N_2As$ H_2O H_2O, 4.69. Found: 5.40.
Subs., anhydrous, 0.1532; 10.2 cc. N (21.5°, 750 mm.).
Calc for $C_{14}H_{15}O_6N_2As$ N, 7.65. Found: 7.62

***m*-Carboxamidophenyl-glycyl-*p*-arsanilic Acid,** *m*-$H_2NCOC_6H_4NHCH_2CONHC_6H_4AsO_3H_2(p)$.—After one hour 5.5 g. of *m*-aminobenzamide[1] yielded an oil on cooling which readily crystallized, giving 10.5 g. of the crude arsonic acid. The neutral solution of the crude acid in dil. sodium hydroxide was salted out with several volumes of saturated sodium acetate solution, and the *sodium salt* recrystallized by treating its warm concentrated solution with alcohol until a slight permanent turbidity remained. Under these conditions the salt crystallized as radiating masses of flat needles containing one molecule of water of crystallization.

Subs., air-dry, 0.6223; loss, 0.0276 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{15}H_{15}O_6N_3AsNa$ H_2O: H_2O, 4.16. Found 4.44.
Subs., anhydrous, 0.2967; (Kjeldahl) 21.3 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1098.
Calc. for $C_{15}H_{15}O_6N_3AsNa$. N, 10.13; As, 18.06. Found: N, 10.06; As, 17.87.

On treating a hot solution of the sodium salt with acetic acid, the *arsonic acid* gradually separated on scratching as microscopic needles. It is very difficultly soluble in boiling water or acetic acid but dissolves somewhat more easily in boiling 50% alcohol. When rapidly heated to 245°, then slowly, it darkens and then decomposes at 248°.

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[1] THIS JOURNAL, 39, 1438 (1917).

Subs., 0.2137 (Kjeldahl); 23.0 cc 0.1 *N* HCl.
Calc. for $C_{15}H_{16}O_5N_3As$: N, 10.68. Found 10.76

***N*-Phenylglycineanilide-*m*-carboxureide-*p*′-arsonic Acid,** *p*-H_2O_3As-$C_6H_4NHCOCH_2NHC_6H_4CONHCONH_2(m)$. — Starting with 5.4 g. of *m*-aminobenzoylurea[1] a clear solution was rapidly obtained and the arsonic acid was deposited during the heating. After cooling and filtering the acid was suspended in a little water, treated with a very slight excess of sodium hydroxide and filtered from a little insoluble material after exactly neutralizing with acetic acid. The addition of powdered, crystalline sodium acetate to the filtrate yielded the *sodium salt*. This was dissolved in a small volume of hot water and treated with an equal volume of alcohol. On standing in the cold the salt separated as flat, microscopic needles containing 3 molecules of water of crystallization. The yield was 7.3 g.

Subs., air-dry, 0.5948, loss, 0.0625 *in vacuo* at 100° over H_2SO_4
Calc. for $C_{16}H_{16}O_6N_4AsNa.3H_2O$: H_2O, 10.55. Found 10.50
Subs., anhydrous, 0.1443: 15.35 cc N (23.0°, 756 mm.)
Subs., 0.3214, $Mg_2As_2O_7$, 0.1073
Calc. for $C_{16}H_{16}O_6N_4AsNa$: N, 12.23, As, 16.36. Found: N, 12.21, As, 16.11.

On adding acetic acid to a dilute solution of the salt the *free acid* separated slowly as spherules of microscopic needles which darken when rapidly heated and decompose at about 280°. The acid is almost insoluble in boiling water or 50% alcohol.

Subs., 0.1441; 15.8 cc. N (20.0°, 758 mm.)
Calc. for $C_{16}H_{17}O_6N_4As$: N, 12.84. Found: 12.74.

***p*-Carboxamidophenyl-glycyl-*p*-arsanilic Acid,** *p*-$H_2NCOC_6H_4NHCH_2$-$CONHC_6H_4AsO_3H_2(p)$.—This substance, prepared from 5.5 g. of *p*-aminobenzamide,[2] separated from the boiling reaction mixture within a few moments, the heating being continued on the water bath for one hour longer and the arsonic acid then filtered off, washed with water and alcohol, and dried. The yield was 13 g. It was suspended in about 100 cc. of warm water, dissolved by neutralizing with sodium hydroxide, and the solution filtered and let stand in the ice box. 13 g. of the *sodium salt* separated as glistening platelets containing 2 molecules of water of crystallization. The salt is quite sparingly soluble in ice water, more easily on warming.

Subs., air-dry, 1.0357, loss, 0.0857 *in vacuo* at 100° over H_2SO_4
Calc. for $C_{15}H_{15}O_5N_3AsNa.2H_2O$: H_2O, 7.99. Found: 8.27
Subs., anhydrous, 0.2995; (Kjeldahl) 21.3 cc. 0.1 *N* HCl, $Mg_2As_2O_7$, 0.1135.
Calc. for $C_{15}H_{15}O_5N_3AsNa$: N, 10.13, As, 18.06. Found: N, 9.96; As, 18.29.

Addition of acetic acid to the filtrate from the sodium salt gave a small amount of the *free acid* as microscopic prisms which do not melt below 275° and are practically insoluble in boiling water or 50% alcohol.

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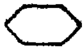
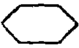
[1] This Journal, 39, 1439 (1917).

[2] *Ibid.*, 39, 1436 (1917), paragraph 2.

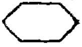
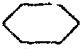
Subs., 0.2075; (Kjeldahl) 15.6 cc. 0.1 *N* HCl.
Calc. for $C_{15}H_{16}O_5N_3As$: N, 10.69. Found: 10.53.

***N*-Phenylglycineanilide-*p*-acetamide-*p'*-arsonic Acid,** H_2O_3As  $NHCOCH_2NH$  CH_2CONH_2. — (From *p*-aminophenyl-acetamide.[1]) The oil which separated on cooling soon crystallized on rubbing, and after dilution of the mixture with water, the crude substance was filtered off, washed, and dissolved in dilute aqueous ammonia. On adding a slight excess of acetic acid an amorphous impurity quickly separated. This was filtered off, after which the pure acid separated slowly as aggregates of microscopic platelets which darken and soften above 180° and decompose completely at 256–8°. It dissolves with difficulty in boiling water, more easily in boiling 50% alcohol or acetic acid.

Subs., 0.1360, 12.0 cc. N (25.5°, 761 mm.) Subs., 0.3214; $Mg_2As_2O_7$, 0.1210.
Calc. for $C_{16}H_{18}O_5N_3As$. N, 10.32; As, 18.41. Found N, 10.11, As, 18.17

***N*-Phenylglycinanilide-*p*-acetureide-*p'*-arsonic Acid,** $H_2O_3AsC_6H_4NHCOCH_2NHC_6H_4CH_2CONHCONH_2$. — (From *p*-amino-phenylacetyl-urea.[2]) The clear solution which immediately formed on boiling set after a few minutes to a solid mass of crystals and it was necessary to continue the heating on the water bath. After diluting with water, the crude product was filtered off, washed, taken up in a little hot water, and treated with sodium carbonate until faintly alkaline. The insoluble, gelatinous residue was collected with bone black and the filtrate treated with sodium acetate until the sodium salt of the arsonic acid began to separate. The salt was converted into the free acid by addition of acetic acid to its hot, dilute solution. The product so obtained was further purified by reprecipitating its very dilute, hot, ammoniacal solution with acetic acid. The pure arsonic acid separated slowly as rosets of microscopic hairs which contained 0.5 molecule of water of crystallization. The anhydrous compound darkens above 230° and decomposes at 270–3°. It is sparingly soluble in boiling water or 50% alcohol.

Subs., air-dry, 0.5047; loss, 0.0094 *in vacuo* at 100° over H_2SO_4
Calc. for $C_{17}H_{19}O_6N_4As.0.5H_2O$: H_2O, 1.96. Found. 1.86.
Subs., anhydrous, 0.1409; 15.3 cc N (22.0°, 756 mm.) Subs., 0.2920, $Mg_2As_2O_7$, 0.1017.
Calc. for $C_{17}H_{19}O_6N_4As$: N, 12.45; As, 16.64. Found. N, 12.49; As, 16.81.

***N*-Phenylglycineanilide-*p*-hydroxyacetic Ether Acid-*p'*-arsonic Acid,** H_2O_3As  $NHCOCH_2HN$  OCH_2COOH. — 3 g. of chloroacetyl-arsanilic acid and 2 g. of *p*-aminophenoxyacetic acid[3] were dissolved in 20 cc. of *N* sodium hydroxide solution and boiled for $^1/_2$ hour. The crude reaction product was filtered off and recrystallized from 50%

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[1] This Journal, 39, 1444 (1917)
[2] *Ibid.*, 39, 2433 (1917).
[3] *Ibid.*, 39, 2196 (1917).

acetic acid, separating as minute, pale brown, wedge-shaped plates containing 1.5 molecules of water of crystallization. The acid is almost insoluble in boiling water or 50% alcohol, and when anhydrous darkens above 180° and decomposes at about 275°.

Subs., air-dry, 0.6434, loss 0.0404, *in vacuo* at 100° over H_2SO_4

Calc. for $C_{16}H_{17}O_7N_2As.1.5H_2O$: H_2O, 5.99. Found: 6.28.

Subs., anhydrous, 0.3070, (Kjeldahl) 14.9 cc. 0.1 *N* HCl. Subs., 0.3300: $Mg_2As_2O_7$, 0.1205.

Calc. for $C_{16}H_{17}O_7N_2As$: N, 6.61; As, 17.67. Found: N, 6.80; As, 17.62.

N-**Phenylglycineanilide-*p*-hydroxyacetic Ether Acid Amide-*p*'-arsonic Acid,** *p*-$H_2O_3AsC_6H_4NHCOCH_2NHC_6H_4OCH_2CONH_2(p)$.—(From 4 g. of *p*-amino phenoxyacetamide.[1]) The new arsonic acid separated almost at once and after heating on the water bath for an hour longer it was filtered off and washed with water. A suspension of the acid in a small volume of water was treated with a very slight excess of sodium hydroxide, quickly made exactly neutral to litmus with acetic acid, and the dark solution filtered. After adding sodium acetate to the filtrate the *sodium salt* separated on standing and was filtered off, dissolved in a little water, and reprecipitated with one to two volumes of alcohol. It crystallized in slightly grayish rosets of flat, glistening needles which, after washing with 85% alcohol and air-drying, contained 4 molecules of water of crystallization. The yield was 3.2 g. A dilute, aqueous solution of the salt gives immediate precipitates with silver or copper ions, a slow-forming, crystalline precipitate with Ca^{++}, and no precipitate with Ba^{++}.

Subs., air-dry, 0.5303, loss, 0.0720 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{16}H_{1}O_6N_3AsNa.4H_2O$: H_2O, 13.93. Found: 13.57.

Subs. anhydrous, 0.1465: 12.4 cc. N (24.0°, 750 mm.). Subs., 0.3069: $Mg_2As_2O_7$, 0.1055.

Calc. for $C_{16}H_{1}O_6N_3AsNa$: N, 9.44; As, 16.84. Found: N, 9.61; As, 16.59.

The *free acid* obtained from the salt with acetic acid separates slowly as woolly masses of delicate needles which are practically insoluble in boiling water or 50% alcohol and which darken somewhat but do not melt below 265°.

Subs., 0.1484, (Kjeldahl) 10.45 cc. 0.1 *N* HCl.

Calc. for $C_{16}H_{18}O_6N_3As$: N, 9.93. Found: 9.87.

N-**Phenylglycineanilide-*p*-hydroxyacetic Ether Acid Ureide-*p*'-arsonic Acid,** *p*-$H_2O_3AsC_6H_4NHCOCH_2NHC_6H_4OCH_2CONHCONH_2$.—Starting with 2.2 g. of *p*-amino-phenoxyacetylurea,[2] the new arsonic acid separated during the heating. The washed product was dissolved in hot, dil. sodium acetate solution, filtered, and saturated sodium acetate solution added to the filtrate until crystallization of the *sodium salt* started. For final purification this was dissolved in a little hot water and the solution treated with alcohol until crystallization again started. After letting stand in the cold the salt was filtered off, washed with 85% alcohol, and air-dried. As so obtained it forms rosets of minute leaflets which contain 4 molecules of water of crystallization.

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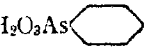
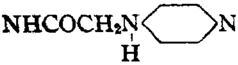
[1] THIS JOURNAL, 39, 2423 (1917).

[2] *Ibid.*, 39, 2435 (1917).

Subs., air-dry, 0.4633; loss, 0.0595 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{17}H_{18}O_7N_4AsNa.4H_2O$: H_2O, 12.86. Found: 12.84.
Subs., anhydrous, 0.1575; 15.4 cc N (22.0°, 764 mm.).
Calc. for $C_{17}H_{18}O_7N_4AsNa$: N, 11.48. Found. 11.38.

On acidification of a hot solution of the salt with acetic acid the *free acid* was obtained as feathery aggregates of minute platelets which are almost insoluble in boiling water or 50% alcohol. When rapidly heated to 255°, then slowly, the acid decomposes at 257-8° with preliminary darkening.

Subs., 0.1680; (Kjeldahl) 14.25 cc 0.1 *N* HCl Subs., 0.3140, $Mg_2As_2O_7$, 0.1034.
Calc. for $C_{17}H_{19}O_7N_4As$. N, 12.02; As, 16.07 Found N, 11.88, As, 15.89

***N*-Phenylglycineanilide-*p*-glycineamide-*p*′-arsonic acid,** $H_2O_3AsC_6H_4NHCOCH_2N(H)C_6H_4NHCH_2CONH_2$.—Carefully purified *p*-aminophenylglycineamide[1] yielded a thick oil which slowly crystallized on rubbing and letting stand, and in subsequent preparations crystallization could be immediately induced by seeding and continued warming on the water bath. The mixture was filtered hot in order to eliminate the tar which separated from the filtrate on cooling. The arsonic acid was washed with hot water, suspended in a considerable volume of hot water, and dissolved by adding ammonia. The solution was then treated with bone black, and on adding acetic acid to the yellow filtrate the arsonic acid separated on standing overnight. It forms crusts of spherical aggregates of micro-crystals which become ochreous in color on exposure to the air. When air-dried it contains approximately 1.5 molecules of water of crystallization. The anhydrous substance darkens at about 200° but does not melt below 285°, and is rather sparingly soluble in boiling water or 50% alcohol.

Subs., air-dry, 0.7072; loss, 0.0468 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{16}H_{19}O_5N_4As.1.5H_2O$: H_2O, 6.02. Found. 6.62.
Subs., anhydrous, 0.1522; (Kjeldahl) 13.90 cc 0.1 *N* HCl Subs., 0.2610; $Mg_2As_2O_7$, 0.0990
Calc. for $C_{16}H_{19}O_5N_4As$ N, 13.27; As, 17.75. Found N, 12.78; As, 18.31.

***N*-Phenylglycineanilide-4,4′-diarsonic acid,** $H_2O_3AsC_6H_4NHCH_2CO-NHC_6H_4AsO_3H_2$.—4.4 g. of arsanilic acid and 6 g. of chloroacetylarsanilic acid were dissolved in 40 cc. of *N* sodium hydroxide solution (2 mols.) and boiled for 30 minutes, during which the product began to separate. After cooling, the mixture was treated with an excess of hydrochloric acid to complete the separation. The substance was purified by redissolving in dilute alkali and reprecipitating with hydrochloric acid. It separated at once as sheaves of microscopic needles, which contain one-half molecule of water of crystallization. The anhydrous substance does not melt up to 280°. It is insoluble in boiling water and very sparingly soluble in hot 50% alcohol

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[1] This Journal, 39, 1459 (1917).

Subs., air dry, 0.6798, loss, 0.0103 *in vacuo* at 100° over H_2SO_4

Calc for $C_{14}H_{16}O_7N_2As_2 \cdot 0.5H_2O$ H_2O, 1.86 Found 1.52

Subs., anhydrous, 0.3313, (Kjeldahl) 13.4 cc 0.1 *N* HCl, $Mg_2As_2O_7$, 0.2195

Calc for $C_{14}H_{16}O_7N_2As_2$ N, 5.91, As, 31.62 Found N, 5.67, As, 31.98

***p*-Acetophenyl-glycyl-*p*-arsanilic acid,** *p*-$CH_3COC_6H_4NHCH_2CONHC_6H_4AsO_3H_2(p)$.—2.8 g of *p*-aminoacetophenone yielded the yellow arsonic acid after a few minutes and the heating was continued on the water bath for $^1/_2$ hour. The collected solid was suspended in a moderate amount of hot water, treated with sodium hydroxide until faintly alkaline, filtered, and the acid reprecipitated from the hot solution with acetic acid. The purified product was again suspended in hot water, dissolved as above, and the solution treated with sodium acetate until the *sodium salt* of the arsonic acid began to separate. After cooling and washing with cold water the yield was 4.5 g. Recrystallized from water, in which it is sparingly soluble in the cold, the salt forms minute, narrow, pale yellow, glistening, platelets containing 3 molecules of water of crystallization.

Subs., air-dry, 1.0979, loss, 0.1258, *in vacuo* at 100° over H_2SO_4

Calc for $C_{16}H_{16}O_6N_2AsNa \cdot 3H_2O$ H_2O, 11.54 Found 11.46

Subs., anhydrous, 0.1620 9.85 cc N (24.0°, 762 mm). Subs., 0.3201, $Mg_2As_2O_7$, 0.1187

Calc for $C_{16}H_{16}O_6N_2AsNa$ N, 6.76, As, 18.09 Found N, 7.00, As, 17.88.

The pure *acid* was obtained from a hot, dilute solution of the sodium salt with acetic acid. It forms radiating masses of faintly yellow, microscopic needles which darken and decompose partially when heated, but do not melt below 290°. The acid is practically insoluble in boiling water and only very sparingly so in boiling 50% alcohol.

Subs., 0.1323, 8.25 cc N (24.0° 765 mm).

Calc for $C_{16}H_{17}O_6N_2As$ N, 7.15 Found 7.22.

NEW YORK, N. Y.

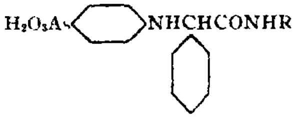
[CONTRIBUTION FROM THE LABORATORIES OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH.]

AROMATIC ARSENIC COMPOUNDS. VI. *N*-(PHENYL-4-ARSONIC ACID)-α-PHENYLGLYCINE AND ITS AMIDES.

BY WALTER A. JACOBS AND MICHAEL HEIDELBERGER

Received July 2, 1919

As a special extension of the general type of substances represented by the substituted amides, ureides and anilides of the phenylglycine arsonic acids,[1] *N*-(phenyl-4-arsonic acid)-α-phenylglycine,



its amide, ureide and a few of the substituted anilides were prepared and studied. With the exception of the glycine itself, which was obtained by hydrolysis of the amide, these substances were made from sodium arsanilate and the phenylchloroacetyl-amino compounds. It was necessary in every case to employ sodium iodide in 50% alcoholic solution in order to accelerate the condensation, since the chloro compounds alone showed little tendency to react.

The general properties of this group of substances resemble those of the simpler glycine derivatives.

Experimental.

***N*-(Phenyl-4-arsonic Acid)-α-phenylglycine,** p-$H_2O_3AsC_6H_4NHCH\cdot(C_6H_5)CO_2H$.—Although this substance unquestionably could be prepared from arsanilic acid and α-phenylchloroacetic acid just as phenylglycine p-arsonic acid has been prepared, we have obtained it by hydrolysis of the corresponding amide described below, and which we had previously prepared.

30 g. of the sodium salt of *N*-(phenyl-4-arsonic acid)-α-phenylglycineamide were dissolved in about 5 parts of 10% sodium hydroxide solution and boiled for about 15 minutes, after which the evolution of ammonia ceased. On adding hydrochloric acid to the chilled solution until acid to congo red the free arsonic acid separated as a colorless oil which rapidly crystallized. The compound was recrystallized from a large volume of boiling water, forming lustrous, rhombic plates. The yield was 20 g. When rapidly heated to 195°, then slowly, the acid darkens and sinters, and finally effervesces at 202-3°. It is sparingly soluble in the cold in water, alcohol or acetic acid, but dissolves more readily on warming. It is more easily soluble in methyl alcohol.

Subs., 0.2077 (Kjeldahl), 6.1 cc 0.1 *N* HCl. Subs., 0.2674; $Mg_2As_2O_7$, 0.1168.
Calc for $C_{14}H_{14}O_5NAs$: N, 3.99, As, 21.36. Found N, 4.11, As, 21.10.

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[1] THIS JOURNAL, 41, 1585 (1919).

***N*-(Phenyl-4-arsonic Acid)-α-phenylglycineamide,** *p*-$H_2O_3AsC_6H_4NH$-$CH(C_6H_5)CONH_2$.—87 g. of arsanilic acid dissolved in 400 cc. of *N* sodium hydroxide solution, 80 g. of sodium iodide, 68 g. (1 mol.) of phenylchloroacetamide, and 500 cc. of alcohol were boiled for 4 hours. The mixture set to a solid cake on cooling. This was disintegrated and stirred with dil. hydrochloric acid until acid to congo red The crude arsonic acid obtained in this way was purified through the sodium salt as described below. On dissolving a portion of this in water and adding acetic acid the free arsonic acid gradually separates as microscopic needles which do not melt below 280°. The substance is sparingly soluble in boiling water or 50% alcohol and practically insoluble in the cold.

Subs., 0.3260 (Kjeldahl), 19.05 cc. 0.1 *N* HCl Subs., 0.3055, $Mg_2As_2O_7$, 0.1337.
Calc. for $C_{14}H_{15}O_4N_2As$: N, 8.00, As, 21.39 Found: N, 8.19, As, 21.12

Sodium Salt.—The crude, washed acid was suspended in warm water, stirred, and treated with 50% sodium hydroxide solution until clear. After exactly neutralizing to litmus with acetic acid the warm solution was filtered, stirred, and treated with powdered sodium acetate until crystallization of the arsonate began. After standing in the ice-box overnight the salt was filtered off, washed first with 20% sodium acetate solution, then with alcohol, and finally recrystallized from alcohol, forming granular aggregates of plates. The yield of air-dried salt was 76 g., the amount of water of crystallization varying from 3.5 to 5 molecules in different preparations. The salt dissolves readily in water or boiling alcohol.

Prepn. 1. Subs., air dry, 0.3384, loss, 0.0659 *in vacuo* at 100° over H_2SO_4
Prepn. 2. Subs., 0.6091, loss, 0.0931
Calc. for $C_{14}H_{14}O_4N_2AsNa.3.5H_2O$: H_2O, 14.48. For $5H_2O$: H_2O, 19.48
Found. Prepn. 2: H_2O, 15.28. Prepn. 1: H_2O, 19.47
1—Subs., anhydrous, 0.2592, (Kjeldahl) 13.80 cc. 0.1 *N* HCl
2—Subs., anhydrous, 0.1577, 10.6 cc. N (25.5°, 758 mm.) Subs., 0.3242; $Mg_2As_2O_7$, 0.1335.
Calc. for $C_{14}H_{14}O_4N_2AsNa$: N, 7.53; As, 20.13 Found: N, 7.46, 7.67. As, 19.88.

***N*-(Phenyl-4-arsonic acid)-α-phenylglycineureide,** *p*-$H_2O_3AsC_6H_4NH$-$CH(C_6H_5)CONHCONH_2$.—4.4 g. of arsanilic acid, 5.3 g. (1.25 mols) of phenylchloroacetyl-urea,[1] 4 g. of sodium iodide, 21 cc. of *N* sodium hydroxide solution, and 22 cc. of alcohol were boiled on the water bath for two hours. On cooling, acidifying to congo red, and rubbing, the glycineureide crystallized. The collected substance was purified by suspending in water, adding sodium hydroxide until faintly alkaline to litmus, filtering, diluting with hot water, and acidifying with acetic acid. The arsonic acid gradually separates in radiating masses of microscopic needles which contain one molecule of water of crystallization when air-dried. When rapidly heated the anhydrous substance swells and evolves gas at 195–7°. It is soluble in boiling water or 50% alcohol, but sparingly so in the cold. The yield was 3.5 g.

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[1] THIS JOURNAL, 39, 2433 (1917).

Subs., air-dry, 0.4267; loss, 0.0199, *in vacuo* at 100° over H_2SO_4

Calc. for $C_{15}H_{16}O_5N_3As.H_2O$ H_2O, 4.38 Found 4.66

Subs. anhydrous, 0.3048 (Kjeldahl); 23.1 cc 0.1 *N* HCl Subs., 0.3045, $Mg_2As_2O_7$, 0.1196.

Calc. for $C_{15}H_{16}O_5N_3As$ N, 10.69, As, 19.06 Found N, 10.62; As, 18.95.

N-**(Phenyl-4-arsonic Acid)-α-phenylglycine-3′-hydroxyanilide,** *p*-$H_2O_3AsC_6H_4NHCH(C_6H_5)CONHC_6H_4OH$(*m*-).—10.5 g. of *m*-phenylchloroacetyl-aminophenol,[1] were employed as in the previous cases. The resulting purple solution was diluted with water and decanted from the gummy precipitate, which was digested on the water bath with hot water. As crystallization could not be induced the mixture was set aside for about a month, when crystals began to form. The process was accelerated by warming and stirring, and the crystals were finally filtered from the hot solution and washed with hot water. The dark purple product was recrystallized twice from 50% alcohol, separating slowly as purplish, lenticular, microscopic platelets, which contain 1.5 molecules of water of crystallization when air-dry and effervesce at 155–60°. The yield was 4.5 g. When rapidly heated to 155°, then slowly, the anhydrous arsonic acid softens at about 155–60° and melts and evolves gas at about 200–10°. It is appreciably soluble in methyl alcohol, and in dilute, as well as strong alcohol. It melts in boiling water, in which it is appreciably soluble, and separates on cooling as an emulsion. It is insoluble in hot acetone.

Subs., air-dry, 0.5600, loss, 0.0333, *in vacuo* at 100° over H_2SO_4

Calc. for $C_{20}H_{19}O_5N_2As$ 1.5H_2O H_2O, 5.76 Found 5.95

Subs. anhydrous, 0.0917, 5.0 cc N (20.8°, 756 mm.) Subs., 0.3040, $Mg_2As_2O_7$, 0.1056

Calc. for $C_{20}H_{19}O_5N_2As$ N, 6.34, As, 16.96. Found N, 6.31, As, 16.76

N-**(Phenyl-4-arsonic Acid)-α-phenylglycine-4′-uraminoanilide,** *p*-$H_2O_3AsC_6H_4NHCH(C_6H_5)CONHC_6H_4NHCONH_2$(*p*-). — The condensation of arsanilic acid and *p*-phenylchloroacetyl-aminophenyl-urea[1] (12.2 g.) was effected exactly as in the preceding example. Crystallization of the product, which started on cooling and scratching, was complete after 24 hours. After washing with 50% alcohol the substance was dissolved in dil. sodium hydroxide, the solution neutralized to litmus with acetic acid, filtered, diluted with hot water, and acidified with acetic acid. The arsonic acid separated as a gummy mass which gradually hardened and was then filtered off and washed with water. The yield was 11 g., decomposing after drying *in vacuo* at 100° at about 255° with preliminary darkening and softening. It dissolves in boiling 50% alcohol, but is very difficultly soluble in boiling water.

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[1] THIS JOURNAL, 39, 1445 (1917).

Subs., 0.1414; 14.2 cc. N (23.0°, 764 mm.). Subs., 0.3575; $Mg_2As_2O_7$, 0.1134.

Calc for $C_{21}H_{21}O_6N_4As$: N, 11.57; As, 15.49. Found: N, 11.65; As, 15.31.

***N*-(Phenyl-4-arsonic acid)-α-phenylglycine-3′-carbamidoanilide,** *p*-$H_2O_3AsC_6H_4NHCH(C_6H_5)CONHC_6H_4CONH_2$(*m*-).—5.9 g. of *m*-phenylchloroacetyl-aminobenzamide,[1] gradually yielded a clear solution. After 4 hours the arsonic acid separated on rubbing, and was washed with 50% alcohol. It was then suspended in water and ammonia added in excess, and the solution treated with bone black to remove the turbidity. The filtrate was diluted to large volume with hot water and acidified with acetic acid, whereupon the acid gradually separated on scratching in microcrystalline form and in a yield of 7 g. It darkens and softens slightly above 250°, melts with effervescence at 261–2°, and is practically insoluble in boiling water or 50% alcohol.

Subs., 0.1431, 11.3 cc. N (23.5°, 760 mm.). Subs., 0.3522, $Mg_2As_2O_7$, 0.1183.

Calc for $C_{21}H_{20}O_5N_3As$: N, 8.96, As, 15.97. Found: N, 9.09, As, 16.20.

***N*-(Phenyl-4-arsonic Acid)-α-phenylglycyl-4-aminophenylacetamide,** *p*-$H_2O_3AsC_6H_4NHCH(C_6H_5)CONHC_6H_4CH_2CONH_2$(*p*-).—The reaction mixture, containing 6.1 g. of α-phenylchloroacetyl-*p*-aminophenylacetamide,[1] was boiled for 3 hours, quickly becoming clear. Dilution with several volumes of water caused the deposition of a thick oil which began to crystallize after a few days. The process was hastened by warming the mixture on the water bath and rubbing, after which the substance was filtered off hot and washed with hot water. The crude product was dissolved in very dilute ammonia, treated with bone black, and the filtrate warmed on the water bath and gradually treated with an excess of acetic acid, seeding at the same time with a crystal of the crude substance and rubbing with a rod. In this way partial separation as an oil was avoided. The yield was 6 g. The arsonic acid was recrystallized from 50% alcohol, forming minute plates and flat needles which contain ½ molecule of water of crystallization. When anhydrous it turns yellow and softens on heating, melting with decomposition at 222–3°. It is sparingly soluble in boiling water and somewhat more easily in boiling 50% alcohol.

Subs., air-dry, 0.5309; loss, 0.0086, *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{22}H_{22}O_6N_3As.0.5H_2O$: H_2O, 1.62. Found: 1.82.

Subs., anhydrous, 0.1366; 10.3 cc. N (21.0°, 769 mm.). Subs., 0.3015; $Mg_2As_2O_7$, 0.0956.

Calc for $C_{22}H_{22}O_5N_3As$: N, 8.70, As, 15.52. Found: N, 8.87; As, 15.30.

NEW YORK, N. Y.

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[1] THIS JOURNAL, 39, 1445 (1917).

[CONTRIBUTION FROM THE LABORATORIES OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH.]

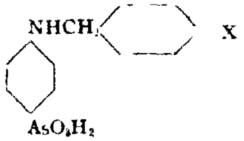
AROMATIC ARSENIC COMPOUNDS. VII. SUBSTITUTED BENZYL, PHENOXYETHYL, AND PHENACYLARSANILIC ACIDS.

BY WALTER A. JACOBS AND MICHAEL HEIDELBERGER.

Received July 2, 1919.

The preceding papers of this series have demonstrated that the reactivity of the amino group in arsanilic acid with chloroacetylamino compounds is such as to render possible the synthesis of a very extensive series of aromatic arsonic acids. It was thought possible that still other series, capable of similar extensive development, might be obtained by the use of other aromatic compounds containing suitable alkyl halide side chains. The present paper is a report of a few attempts in this direction which represent merely a beginning in the study of such substances, the pressure of other work having temporarily limited the development of these types of compounds.

Benzyl chloride and the substituted benzyl chlorides were found to react with sodium arsanilate under suitable conditions to form benzyl and substituted benzylarsanilic acids,



Although long boiling of the solution in 50% alcohol was required with benzyl chloride itself in order to obtain the greatest yields, owing to the stability of the halogen in this substance, the reaction proceeded far more easily and completely in the case of the negatively substituted benzyl halides such as *p*-nitrobenzyl chloride, 3-nitro-4-hydroxybenzyl chloride, *p*-carboxybenzyl chloride and *p*-carboxamidobenzyl chloride, the halogen of which is very reactive. The arsonic acids obtained from the above nitrobenzyl chlorides were reduced to the corresponding aminobenzyl arsanilic acids by means of ferrous hydroxide, a method which we have found to be especially serviceable for the selective reduction of nitroarsonic acids.[1]

Another group of substances studied was those obtained by reacting sodium arsanilate with phenoxyethyl bromide and such of its derivatives as salicylamide-bromoethyl ether and *p*-acetamino-phenoxyethyl bromide.

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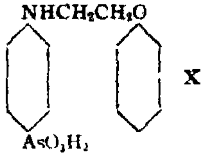
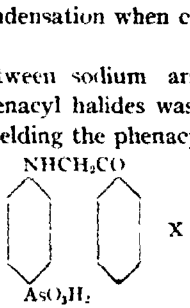
[1] Cf. THIS JOURNAL, 40, 1580 (1918).



The reaction was found to proceed very slowly and incompletely in boiling 50% alcoholic solution even in the presence of sodium iodide which strongly accelerated the condensation when chloroacetyl compounds were in question.

Finally, the reaction between sodium arsanilate and halogen-acetyl compounds such as the phenacyl halides was studied and found to proceed in the desired sense, yielding the phenacyl-arsanilic acids



These compounds are yellow in color and yield yellow solutions.

All of the above groups of substances function both as acids and feeble bases, forming salts with alkalies and strong mineral acids. With the exception of the negatively substituted benzyl derivatives they are readily displaced from their alkali salts by a slight excess of acetic acid.

Experimental.

(A) Benzyl-*p*-arsanilic Acids.

Benzyl-arsanilic Acid, *p* $C_6H_5CH_2NHC_6H_4AsO_3H_2$.—4.4 g. of arsanilic acid were dissolved in 20 cc. of *N* sodium hydroxide solution and boiled under a reflux condenser for 4 hours with 2.7 g. of benzyl chloride, 1.5 g. of sodium iodide, and 20 cc. of alcohol. The benzylarsanilic acid separated during the heating and was washed with 50% alcohol, and finally with ether. The yield was 4.3 g. The crude substance was dissolved in dil. sodium hydroxide, treated with bone black, and precipitated while hot with acetic acid, the arsonic acid separating quickly as flat, lustrous, microscopic needles. For analysis it was best recrystallized from hot 50% alcohol, in which it is fairly readily soluble, forming arborescent masses of micro-crystals and larger prisms. The acid decomposes at about 255° with preliminary sintering, and is very sparingly soluble in hot water. Although difficultly soluble in the cold, boiling alcohol and acetic acid readily dissolve the substance. It is also soluble in methyl alcohol at room temperature and is insoluble in 10% hydrochloric acid, but stronger acid dissolves it. On adding sodium nitrite to a solution of the compound in hot acetic acid, cooling and rubbing, yellow spherules of microscopic crystals, presumably the nitroso compound, separate. On concentrating a neutral solution of the arsonic acid in aqueous sodium hydroxide to small volume and cooling, the *sodium salt* separates as glistening platelets which dissolve readily on dilution.

Subs., 0.2067; (Kjeldahl) 6.7 cc. 0.1 *N* HCl. Subs., 0.2747; $Mg_2As_2O_7$, 0.1378.
Calc. for $C_{13}H_{14}O_3NAs$: N, 4.56; As, 24.41. Found: N, 4.56; As, 24.21.

***p*-Nitrobenzyl-arsanilic Acid,** *p*-$O_2NC_6H_4CH_2NHC_6H_4AsO_3H_2$.—8.8 g. of arsanilic acid in 40 cc. of *N* sodium hydroxide solution, 7 g. of *p*-nitrobenzyl chloride, and 40 cc. of alcohol were boiled for 3 hours, during which the molten chloride gradually disappeared. The yellow crystals which deposited on cooling were washed with 50% alcohol and then with acetone. The yield was 10 g. For purification a hot, dilute alkaline solution of the substance was precipitated with acetic acid. Recrystallized for analysis from hot 85% alcohol, in which it is sparingly soluble, it forms sheaves of flat, yellow, microscopic needles which do not melt when heated up to 280°. The acid is almost insoluble in boiling water and only sparingly so in boiling methyl alcohol or acetic acid.

Subs., 0.1598; 11.0 cc. N (22.5°, 762 mm.). Subs., 0.3023, $Mg_2As_2O_7$, 0.1320.
Calc. for $C_{13}H_{13}O_5N_2As$: N, 7.95, As, 21.28. Found: N, 7.97; As, 21.06.

***p*-Aminobenzyl-arsanilic Acid,** *p*-$H_2NC_6H_4CH_2NHC_6H_4AsO_3H_2$.—40 g. of ferrous sulfate dissolved in 150 cc. of water were treated with 25% sodium hydroxide solution until the mixture remained strongly alkaline to litmus after thorough shaking.[1] Ice was added and then a solution of 7 g. of *p*-nitrobenzyl-arsanilic acid in dil. sodium hydroxide. After 5 minutes' shaking the mixture was filtered, acidification of the filtrate with acetic acid yielding the crystalline amino compound contaminated with an amorphous by-product. For purification the crude substance was dissolved in cold, dil. ammonia, leaving a small amount of amorphous material which was collected in the cold with bone black. Acidification of the clear filtrate yielded the pure amino acid at once as colorless aggregates of microscopic leaflets which decompose at about 202°. The yield was 3.5 g. The acid is practically insoluble in hot water or 50% alcohol. On boiling a solution in dil. ammonia a white, amorphous alteration product is formed which is insoluble in ammonia. This does not happen with fixed alkali. The pure acid is soluble in both alkali and mineral acids, a solution in the latter being readily diazotizable, coupling with R-salt to form a deep red dye.

Subs., 0.1510; 11.9 cc. N (21.0°, 740 mm.). Subs., 0.3241; $Mg_2As_2O_7$, 0.1573.
Calc. for $C_{13}H_{15}O_3N_2As$: N, 8.70; As, 23.28. Found: N, 8.92; As, 23.41.

3-Nitro-4-hydroxybenzyl-arsanilic Acid, 3,4-$(O_2N)HOC_6H_3CH_2NH$-$C_6H_4AsO_3H_2$(*p*-).—To a hot solution of 11 g. of arsanilic acid in 50 cc. of *N* aqueous sodium hydroxide a solution of 9.5 g. of 3-nitro-4-hydroxybenzyl chloride in 50 cc. of hot alcohol was added. The condensation took place rapidly but the heating was continued for 30 minutes. The alcohol was then allowed to boil off, causing the mixture to set to a thick mass of yellow crystals. These were filtered off and washed first with 50% alcohol and finally with acetone, the yield being 15 g. The crude acid was purified over the sodium salt by suspending it in a small volume of hot water and carefully treating with sodium hydroxide until solution was complete. On adding an equal volume of saturated sodium acetate solution to the reddish orange solution the *sodium salt* separated as a thick mass of long, thin, yellow, microscopic needles, which were filtered off and washed with 20% sodium acetate solution. On cautiously adding an excess of acetic acid to a hot, dilute solution of the salt the pure arsonic acid separated as aggregates of microscopic needles containing no water of crystallization. However, when recrystallized from 85% alcohol it crystallizes more slowly, forming crusts of minute, yellow crystals which contain one molecule of water of crystallization. When rapidly heated the anhydrous substance darkens and sinters above 210° and decomposes at about 245–50°. It is practically insoluble in boiling water, sparingly in the cold in alcohol, methyl alcohol, or acetic acid, and readily on boiling.

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[1] *Loc. cit.*

Subs., air-dry, 0.9344; loss, 0.0471, *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{13}H_{13}O_6N_2As.H_2O$: H_2O, 4.66. Found: 5.04.
Subs., anhydrous, 0.2655, (Kjeldahl) 14.5 cc. 0.1 *N* HCl.
Calc. for $C_{13}H_{13}O_6N_2As$: N, 7.61. Found: 7.65.

3-Amino-4-hydroxybenzyl-arsanilic Acid.—9 g. of 3-nitro-4-hydroxybenzylarsanilic acid were dissolved in dil. sodium hydroxide solution and added at once to a ferrous hydroxide suspension prepared by precipitating a solution of 50 g. of ferrous sulfate with sodium hydroxide until it remained strongly alkaline on shaking. After 5 minutes' shaking the mixture was filtered on a large Buchner funnel and the dark brown filtrate acidified with acetic acid, yielding a dark brown, crystalline precipitate of the amino acid on rubbing. For purification this was dissolved in dil. hydrochloric acid and a solution of sodium acetate added as long as the precipitate which first formed redissolved on stirring. A few dark-colored flocks were collected by the addition of bone black and the faintly colored filtrate diluted and treated further with sodium acetate solution until no longer acid to congo red, the arsonic acid separating as almost colorless, microscopic platelets which contained $^1/_2$ molecule of water of crystallization. The yield was 3 g. When heated to 285° the anhydrous substance darkens slightly, but does not melt. It is sparingly soluble in boiling water or 50% alcohol. An alkaline solution darkens rapidly on standing, while an aqueous suspension gives a deep brown color with ferric chloride solution.

Subs. air-dry, 0.6106; loss, 0.0155 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{13}H_{16}O_4N_2As.0.5H_2O$: H_2O, 2.59. Found: 2.54.

Subs., anhydrous, 0.2298; (Kjeldahl) 13.45 cc 0.1 *N* HCl Subs., 0.2565; $Mg_2As_2O_7$, 0.1170.

Calc. for $C_{14}H_{15}O_4N_2As$. N, 8.28, As, 22.18 Found N, 8.20, As, 22.02

***p*-Carboxybenzylarsanilic Acid,** *p*-$HO_2CC_6H_4CH_2NHC_6H_4AsO_3H_2$.—3.5 g. of *p*-carboxybenzyl chloride in 20 cc. of *N* sodium hydroxide solution were added to a solution of 4.4 g. of arsanilic acid in 20 cc. of the same medium. The mixture was gently warmed and stirred until solution was complete and then allowed to stand at room temperature, a crop of crystals soon separating. After 24 hours the crystals were filtered off, dissolved by the addition of dil. sodium hydroxide, and the solution then heated. On adding hydrochloric acid to the hot solution a gum separated which rapidly crystallized. The collected and washed solid was boiled out with alcohol to remove impurities and converted into the *sodium salt* for final purification. After dissolving in dil. sodium hydroxide solution, neutralizing with acetic acid, and concentrating to small bulk, a large volume of alcohol was added to the hot solution, causing the separation of the salt as a colorless, microcrystalline powder. Recrystallized from a concentrated aqueous solution by adding alcohol the salt formed aggregates of flat needles containing approximately $^1/_2$ molecule of water of crystallization. The yield was 2.5 g.

Subs., air-dry, 0.2886, loss, 0.0082 *in vacuo* at 100° over H_2SO_4

Calc. for $C_{14}H_{12}O_5NAsNa_2.0.5H_2O$. H_2O, 2.23 Found 2.84

Subs., anhydrous, 0.3230, (Kjeldahl) 8.3 cc 0.1 *N* HCl, $Mg_2As_2O_7$, 0.1260

Calc. for $C_{14}H_{12}O_5NAsNa_2$. N, 3.55, As, 18.86 Found N, 3.60, As, 18.83

On adding acetic acid to a hot solution of the sodium salt the *free acid* separated as delicate, microscopic needles which did not melt below 280°. It is sparingly soluble in hot 50% alcohol or acetic acid and insoluble in other neutral solvents.

Subs., 0.2397, 8.4 cc N (22.0°, 762 mm). Calc. for $C_{14}H_{14}O_5NAs$ N, 3.99 Found 4.07.

***p*-Carboxamidobenzyl-arsanilic Acid,** *p*-$H_2NCOC_6H_4CH_2NHC_6H_4AsO_3H_2$.—33 g. of arsanilic acid in 150 cc. of *N* aqueous sodium hydroxide, 25.5 g. of *p*-(ω-chloromethyl)benzamide, and 150 cc. of alcohol were boiled for two hours, a thick mass of crystals separating on cooling. After filtering and washing first with water and then with alcohol, the arsonic acid was converted into the *sodium salt.* The solution of the acid in a small volume of warm, dil. sodium hydroxide was carefully neutralized with acetic acid. Separation of the salt, which commenced on cooling, was completed by adding saturated sodium acetate solution. Recrystallized from 50% alcohol the salt forms aggregates of thin plates containing 2.5 molecules of water of crystallization and is easily soluble in water. The yield was 30 g.

Subs., air-dry, 0.6617; loss, 0.0732 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{14}H_{14}O_4N_2AsNa.2.5H_2O$. H_2O, 10.79. Found: 11.08.

Subs., anhydrous, 0.3216, (Kjeldahl) 17.0 cc. 0.1 *N* HCl, $Mg_2As_2O_7$, 0.1329.
Calc. for $C_{14}H_{14}O_4N_2AsNa$: N, 7.53; As, 20.13. Found: N, 7.41; As, 19.95.

Acetic acid added to a hot solution of the salt precipitates the *arsonic acid* as sheaves and plumes of microscopic needles. It does not melt below 280° and is almost insoluble in boiling water, 50% alcohol, or methyl alcohol.

Subs., 0.2308, (Kjeldahl) 13.1 cc. 0.1 *N* HCl.
Calc. for $C_{14}H_{15}O_4N_2As$: N, 8.00. Found: 7.95.

(B) Phenoxyethyl- and Phenacyl-*p*-arsanilic Acids.

Phenoxyethylarsanilic Acid, *p*-$C_6H_5OCH_2CH_2NHC_6H_4AsO_3H_2$.—Phenoxyethyl bromide was found to react very slowly with arsanilic acid, and although condensation was somewhat accelerated by the addition of sodium iodide, long-continued boiling of the reaction mixture was found necessary. A solution of 4.4 g. of arsanilic acid in 20 cc. of *N* aqueous sodium hydroxide, 4 g. of sodium iodide, 4 g. of phenoxyethyl bromide, and 20 cc. of alcohol were boiled for 24 hours. On cooling and diluting with water the reaction product crystallized as glistening leaflets which were filtered off and washed first with water and then with ether to remove unchanged bromide. The yield was 3 g. The acid was converted into the *sodium salt* by dissolving in a small amount of dil. sodium hydroxide solution, exactly neutralizing to litmus with acetic acid, and then treating with dry acetone until a turbidity was produced. On standing in the refrigerator the salt slowly separated as delicate needles. Recrystallized from a small volume of 85% alcohol it forms flat, microscopic needles containing 3.5 molecules of water of crystallization.

Subs., air dry, 0.7668, loss, 0.1119 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{14}H_{15}O_4NAsNa.3.5H_2O$: H_2O, 14.89. Found: 14.59.

On treating the hot solution of the salt with acetic acid the free *arsonic acid* separated as glistening scales containing one molecule of water of crystallization. It is very sparingly soluble in boiling water or acetic acid, but is appreciably soluble in hot methyl alcohol, alcohol, or 50% alcohol. The anhydrous substance does not decompose below 280°.

Subs., air dry, 0.4534, loss, 0.0242 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{14}H_{16}O_4NAs.H_2O$: H_2O, 5.07. Found: 5.34.
Subs., anhydrous, 0.2263, (Kjeldahl) 7.0 cc. 0.1 *N* HCl. Subs., 0.2569, $Mg_2As_2O_7$, 0.1190.
Calc. for $C_{14}H_{16}O_4NAs$: N, 4.16; As, 22.22. Found: N, 4.33; As, 22.37.

***p*-Acetamino-phenoxyethyl-arsanilic Acid,** *p*-$CH_3CONHC_6H_4OCH_2CH_2NHC_6H_4AsO_3H_2$.—Arsanilic acid was condensed as in the previous example with *p*-acetamino-phenoxyethyl bromide. The reaction mixture was diluted with water, made alkaline with sodium hydroxide, filtered from unchanged halide, and acidified with acetic acid, yielding the crystalline arsonic acid. This was converted into the *sodium salt* by solution in a small volume of dil. sodium hydroxide, careful neutralization with acetic acid, and addition of saturated sodium acetate solution. After standing in the refrigerator the sodium salt was filtered off and washed with 20% sodium acetate solution and finally with 85% alcohol. Purified by dissolving in a small volume of water and precipitating with several volumes of alcohol, the salt forms colorless, microscopic platelets which contain about 3 molecules of water of crystallization.

Subs., air-dry, 0.5364; loss, 0.0580 *in vacuo* over H_2SO_4 at 100°.
Calc. for $C_{16}H_{18}O_5N_2AsNa.3H_2O$. H_2O, 11.49. Found· 10.81.
Subs., anhydrous, 0 3250; (Kjeldahl) 15.6 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1225.
Calc. for $C_{16}H_{18}O_5N_2AsNa$: N, 6.73; As, 18.01. Found: N, 6.72; As, 18.20.

On treating a hot solution of the salt with acetic acid the *arsonic acid* separated as delicate, glistening needles and platelets. Recrystallized from 50% alcohol it forms long, thin, narrow plates which do not melt below 275°. It is practically insoluble in boiling water and very difficultly so in hot alcohol or methyl alcohol, but dissolves in hot 50% alcohol or glacial acetic acid.

Subs., 0.2075; (Kjeldahl) 14 95 cc 0 0714 *N* HCl
Calc. for $C_{16}H_{19}O_5N_2As$: N, 7 11 Found 7.21.

o-Carboxamido-phenoxyethyl-arsanilic Acid, *o*-$H_2NCOC_6H_4OCH_2CH_2NHC_6H_4AsO_3H_2$—The reaction mixture, similarly obtained from 10 g. of salicylamide-bromoethyl ether (2-bromoethoxy-benzamide)[1] was diluted with water, made alkaline with sodium hydroxide, filtered, and the filtrate acidified with acetic acid, depositing an amorphous, gelatinous precipitate followed by crystals on long standing in the refrigerator The product was recrystallized from a small volume of hot 50% alcohol, 4 g. of the arsonic acid separating in wedge-shaped, microscopic prisms. For analysis it was again recrystallized from 50% alcohol. The substance is very difficultly soluble in boiling water, and when pure is only sparingly soluble in most hot solvents except hot acetic acid and hot 50% alcohol. When precipitated from its solution in alkali by means of acetic acid it separates slowly as rosets of broad, microscopic needles. When rapidly heated it does not melt below 280°, but if the temperature is held at this point the acid slowly melts and decomposes.

Subs., 0.2930; (Kjeldahl) 15.30 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1185
Calc. for $C_{15}H_{17}O_5N_2As$· N, 7.37; As, 19.62. Found N, 7 32, As, 19.52

Phenacylarsanilic Acid, $C_6H_5COCH_2NHC_6H_4AsO_3H_2$.—4 4 g. of arsanilic acid in 20 cc. of *N* aqueous sodium hydroxide and a solution of 4 g. of ω-bromoacetophenone in 20 cc. of alcohol were boiled for one hour, the arsonic acid crystallizing during the reaction. The yield was 4 g. It was recrystallized by dissolving in dil. sodium hydroxide solution, heating and acidifying, the phenacyl compound separating as faintly yellow, arborescent aggregates of delicate, microscopic needles. It decomposes at 185–7° with preliminary softening and is sparingly soluble in the usual solvents. An alkaline solution is yellow, the color deepening on standing. Conc. sulfuric acid dissolves the substance with a bright yellow color.

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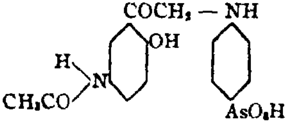
[1] *J. Biol. Chem.*, 21, 449 (1915).

Subs., 0.1711; 6.4 cc. N (21.0°, 766 mm.) Subs., 0.3519, $Mg_2As_2O_7$, 0.1625
Calc. for $C_{14}H_{14}O_6NAs$: N, 4.18, As, 22.36. Found: N, 4.38, As, 22.29

2-Hydroxy-5-acetamino-phenacylarsanilic Acid,



.—A warm solution of 4.4 g. of arsanilic acid in 10 cc. of 2 *N* sodium hydroxide and 10 cc. of alcohol was treated with 5.5 g. of 3-acetamino-6-hydroxyphenacyl bromide.[1] The bromide dissolved rapidly and the mixture was heated on the water bath for an hour. On dilution with water an amorphous precipitate was formed, followed on standing in the refrigerator by a crystalline substance. The precipitate, washed with water and acetone, could not be recrystallized directly from neutral solvents, but purification was finally effected by taking advantage of the weakly basic properties of the arsonic acid. A suspension in 1:1 hydrochloric acid was treated with conc. hydrochloric acid until most of the substance had dissolved, then rapidly filtered, and the dark yellow filtrate treated with several volumes of hot water. Owing to the hydrolysis of its hydrochloride the phenacyl compound separated at once as a dark yellow powder consisting of aggregates of microscopic platelets which redden and decompose at 228°. The yield was only 1.2 g. The acid is practically insoluble in hot water or 50% alcohol and dissolves in conc. sulfuric acid with a reddish brown color.

Subs., 0.2946; (Kjeldahl) 14.5 cc. 0.1 *N* HCl, $Mg_2As_2O_7$, 0.1124
Calc. for $C_{16}H_{17}O_6N_2As$: N, 6.86, As, 18.36. Found: N, 6.89, As, 18.43

NEW YORK, N. Y.

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[1] **3-Acetamino-6-hydroxy-phenacyl Bromide.**—From acetophenetidine, bromoacetyl chloride, and aluminum chloride with exclusion of moisture, similarly to the corresponding chloro compound [Kunckell, *Ber.*, 34, 128 (1901)]. The crude product (95% of the theory) was used for the preparation of the arsonic acid. A portion of the crude bromide was boiled with chloroform and the filtrate treated with ligroin, the bromide separating as a drab-colored precipitate melting at 133–5° with preliminary softening and slight gas evolution to a turbid, red-brown liquid which clears at 136°. The bromide dissolves readily in acetone or alcohol, less easily in boiling chloroform. The yellowish solution in alcohol changes to a deep olive green on addition of a drop of ferric chloride solution, or to orange-red on addition of aqueous sodium hydroxide.

Subs., 0.1785; 7.85 cc. N (21.0°, 758 mm.) Subs., 0.1673, (Carius) AgBr, 0.1179.
Calc. for $C_{10}H_{10}O_3NBr$: N, 5.15; Br, 29.37. Found: N, 5.09; Br, 29.99

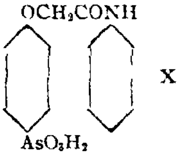
[Contribution from the Laboratories of the Rockefeller Institute for Medical Research.]

AROMATIC ARSENIC COMPOUNDS. VIII. THE AMIDES OF (4-ARSONIC ACID)-PHENOXYACETIC ACID AND THE ISOMERIC PHENOXYACETYL-ARSANILIC ACIDS.

By Walter A. Jacobs and Michael Heidelberger.

Received July 2, 1919.

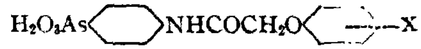
The preparation of *o*-phenylglycollic acid *p*-arsonic acid ([4-arsonic acid]-phenoxyacetic acid) by the action of sodium chloroacetate on sodium *p*-hydroxyphenyl-arsonate in boiling aqueous solution has been described in German patent 216,270. We have found that chloroacetylamino compounds also react with sodium *p*-hydroxyphenyl-arsonate to give the substituted amides of phenylglycollic acid *p*-arsonic acid with the following general formula



In this reaction a condition for the success of the condensation was the addition of an extra molecule of sodium hydroxide in order to form the sodium phenolate, as in the preparation of phenyl ethers with alkyl halides in general. When using chloroacetyl compounds which were sufficiently stable in alkaline solution the yields of the desired products were good, but in those cases in which the halide was readily decomposed the yields suffered accordingly.

In general, the arsonic acids of this type crystallize readily when pure, possess high decomposition points, and are sparingly soluble in the usual solvents. They are stronger acids than the amides of phenylglycinearsonic acid, since only mineral acids or a large excess of acetic acid displace them completely from their salts.

In a preceding paper it was shown that the sodium salt of chloroacetylarsanilic acid reacted smoothly with amines with the formation of substituted glycyl-arsanilic acids.[1] On replacing the amine by a phenolic compound the substituted phenoxyacetyl or phenyl ether glycollyl-arsanilic acids were obtained with the general formula



$$H_2O_3As\langle C_6H_4\rangle NHCOCH_2O\langle C_6H_4\rangle—X$$

These substances are of course isomeric with the amides of (4-arsonic acid)-phenoxyacetic acid. As in the preparation of the latter substances an extra molecule of alkali was required for the conversion of the phenolic compound into the phenolate. Since the reaction of the mixture was, therefore, strongly alkaline, the sensitive chloroacetyl-arsanilic acid suffered partial decomposition, so that the yields of the desired phenoxyacetyl compounds were poorer than in the synthesis of the glycyl-arsanilic acids.

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[1] This Journal, 41, 1809 (1919).

As a rule the phenoxyacetyl-arsanilic acids crystallize readily and are sparingly soluble in the usual solvents, but yield readily soluble sodium salts. They are stronger acids than the glycyl-arsanilic acids and are completely displaced from their salts only by mineral acid or a large excess of acetic acid.

On reduction both of these groups of substances yield arsinoxides and arseno compounds, substances which will be described when our studies with this group are completed.

Experimental.

(A) Derivatives of (4-Arsonic Acid)-phenoxyacetic Acid.

(4-Arsonic Acid)-phenoxyacetic Methyl Ester, *p*-$H_2O_3AsC_6H_4OCH_2CO_2CH_3$.—10 g. of (4-arsonic acid)-phenoxyacetic acid[1] were refluxed for two hours with a mixture of 30 g. of dry methyl alcohol and 3 g. of conc. sulfuric acid. On dilution with water the ester separated in a yield of 9.5 g. Recrystallized from hot water it forms lustrous plates which, when rapidly heated, partially melt with gas evolution at about 192–5° and then gradually decompose at a higher temperature without melting completely. The ester is readily soluble in methyl alcohol, hot ethyl alcohol, or water, but sparingly in cold alcohol or water.

Subs., 0.2967; $Mg_2As_2O_7$, 0.1575

Calc for $C_9H_{11}O_6As$ As, 25.85 Found 25.62

(4-Arsonic Acid)-phenoxyacetamide, *p*-$H_2O_3AsC_6H_4OCH_2CONH_2$.—60 g. of the methyl ester were added slowly, with chilling and shaking, to 360 cc. of conc. ammonia. During the addition the mixture set to a thick mass of what appeared to be the ammonium salt of the unchanged ester and this had to be broken up occasionally during the further addition of the ester. When all had been added the mixture was vigorously shaken to disintegrate the mass as thoroughly as possible and then allowed to stand at room temperature for 24 hours. The ammonium salt changed definitely in character, presumably due to the formation of the ammonium salt of the amide. The mixture was finally diluted with water until solution was complete and the excess of ammonia removed *in vacuo*, after which the solution was made faintly acid to congo red with hydrochloric acid, causing the immediate separation of the arsonic acid. On recrystallization from hot water the amide separated as rhombic, microscopic prisms. The yield was 37.5 g. The compound does not melt below 280° and is sparingly soluble in cold water or hot alcohol, but easily soluble in boiling water.

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[1] Ger. pat. 216.270

Subs., 0.1312; 6.1 cc. N (20.5°, 750 mm.).
Calc. for $C_8H_{10}O_5NAs$: N, 5.09. Found: 5.34.

Sodium Salt.—A solution of the acid in dil. aqueous sodium hydroxide was carefully neutralized with acetic acid and concentrated to small volume *in vacuo*. On adding alcohol the salt separated slowly as glistening platelets which contained no water of crystallization and were easily soluble in water.

Subs., 0.1371; 5.7 cc. N (22.5°, 765 mm.). Subs., 0.3120, $Mg_2As_2O_7$, 0.1617
Calc. for $C_8H_9O_5NAsNa$: N, 4.71, As, 25.23. Found: N, 4.84, As, 25.00.

(4-Arsonic Acid)-phenoxyacetanilide, *p*-$H_2O_3AsC_6H_4OCH_2CONHC_6H_5$.—5 g. of sodium *p*-hydroxyphenyl-arsonate,[1] 3.4 g. of chloroacetanilide,[2] and 3 g. of sodium iodide were boiled in a mixture of 20 cc. of *N* aqueous sodium hydroxide and 20 cc. of alcohol for 3 hours. The alcohol was then allowed to boil off and the residue acidified with hydrochloric acid, resulting in a gummy precipitate which rapidly recrystallized. For purification the collected material was dissolved in dil. sodium hydroxide and the filtrate treated, preferably while hot, with an excess of hydrochloric acid. The arsonic acid separated at once as glistening platelets. When rapidly heated the anilide darkens slightly above 250° but does not melt below 280°. From hot 50% alcohol, in which it is fairly readily soluble, it separates as minute prisms and masses of thin, microscopic plates. Although but sparingly soluble in the cold it is appreciably soluble in hot water, alcohol, and acetic acid. Cold methyl alcohol also dissolves the substance.

Subs., 0.3024, (Kjeldahl) 8.6 cc. 0.1 *N* HCl. Subs., 0.3455, $Mg_2As_2O_7$, 0.1530.
Calc. for $C_{14}H_{14}O_5NAs$: N, 3.99, As, 21.34. Found: N, 3.98, As, 21.37.

(4-Arsonic Acid)-phenoxyacetyl-3-aminophenol, *p*-$H_2O_3AsC_6H_4OCH_2$-$CONHC_6H_4OH(m)$.—43.6 g. of *p*-hydroxyphenyl-arsonic acid[3] dissolved in 400 cc. of *N* sodium hydroxide solution, and 38 g. of *m*-chloroacetylaminophenol[4] were boiled for 15 minutes. During the heating an amorphous substance separated and more of this material was precipitated on dilution with water. The mixture was made definitely acid with acetic acid and cleared by treating with bone black in the cold. On the addition of hydrochloric acid to the filtrate until acid to congo red a pinkish paste separated, but on standing and scratching this was followed by crystals. After 24 hours crystallization was complete. The nitrogen figures obtained with this substance were nearly 1% high and the arsenic figures too low, indicating the presence of a contaminating arsonic acid containing a higher percentage of nitrogen. It is possible that the hydroxyl group in the *m*-aminophenol may have reacted with a second molecule of *m*-chloroacetylamino-phenol giving a more complex arsonic acid. Since direct recrystallization of the crude product from a suitable solvent such as 50% alcohol or 50% acetic acid did not remove this contaminating material it was found necessary to pass through the *sodium salt*, which was fortunately found to have suitable properties.

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[1] This Journal, **41**, 1447 (1919).

[2] *Ibid.*, **39**, 1441 (1917).

[3] *Ibid.*, **41**, 1446 (1919).

[4] *Ibid.*, **39**, 1442 (1917). An improved method will be published shortly.

The crude acid was suspended in a small volume of water and dissolved by the addition of sodium hydroxide solution. After neutralization with acetic acid an equal volume of saturated salt solution was added. On scratching, the pink solution gradually deposited the sodium salt, which carried the color with it. After standing in the refrigerator it was filtered off and washed with 15% salt solution. The crude salt was recrystallized from a small volume of hot water, separating as a mass of pink, lustrous, microscopic needles and long, thin platelets. On dissolving in hot water and adding hydrochloric acid a milky emulsion was formed which almost immediately crystallized. The free acid settled quicky as a heavy, sandy powder consisting of aggregates of irregular, microscopic leaflets to which the pink color still adhered. When rapidly heated it melts and decomposes at 238-40°. It is very sparingly soluble in boiling water or boiling acetic acid but dissolves more readily in hot 50% alcohol.

Subs., 0.2067; (Kjeldahl) 5.85 cc. 0.1 *N* HCl. Subs., 0.3209; $Mg_2As_2O_7$, 0.1375.

Calc. for $C_{14}H_{14}O_6NAs$: N, 3.83; As, 20.42. Found, N, 3.97; As, 20.68.

(4-Arsonic Acid)-phenoxyacetyl-4-aminophenol.—22 g. of *p*-hydroxyphenyl-arsonic acid dissolved in 100 cc. of 2 *N* sodium hydroxide solution (2 mols.), and 19 g. of *p*-chloroacetylamino-phenol[1] were boiled under a reflux condenser. A precipitate separated from the clear solution after a few seconds and was probably an alteration product of the chloroacetyl compound. After 30 minutes the mixture was considerably diluted, acidified with acetic acid, and treated with bone black in the cold. The clear filtrate yielded a crystalline arsonic acid on acidification to congo red with hydrochloric acid and scratching. After 24 hours the collected substance was repurified by reprecipitation of its solution in dil. ammonia with hydrochloric acid. As the analysis showed the product to be high in nitrogen it was finally purified over the *sodium salt*.

The acid was suspended in a small volume of hot water and carefully treated with sodium hydroxide solution until dissolved. On cooling, the colorless sodium salt crystallized and was filtered off, washed, redissolved in hot water and acidified with hydrochloric acid. The arsonic acid separated at once as curved, colorless, microscopic crystals. When rapidly heated it gradually darkens and decomposes at 238-40°. It is very difficultly soluble in boiling water, alcohol, or methyl alcohol, but dissolves more easily in hot 50% alcohol. On adding a few drops of sodium nitrite solution to a suspension of the acid in hot acetic acid a clear, orange solution is obtained which deposits spherules of yellow crystals, probably a nitroso compound, in cooling.

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[1] THIS JOURNAL, 39, 1442 (1917).

Subs., 0.2113; (Kjeldahl) 6.15 cc. 0.1 *N* HCl. Subs., 0.3269; $Mg_2As_2O_7$, 0.1354.
Calc. for $C_{14}H_{14}O_6NAs$: N, 3 83; As, 20 42. Found. N, 4.07; As, 20.00.

(4-Arsonic Acid)phenoxyacetyl-4-aminophenylurea, p-$H_2O_3AsC_6H_4OCH_2CONHC_6H_4NHCONH_2(p\text{-})$.—8.8 g. of *p*-hydroxyphenylarsonic acid in 40 cc. of 2 *N* sodium hydroxide solution, 8 g. of sodium iodide, 9 2 g. of *p*-chloroacetylamino-phenylurea,[1] and 40 cc. of alcohol were refluxed for two hours. After dilution with water an excess of acetic acid was added. On scratching a white powder separated and this was filtered off, dissolved in dil. ammonia, and treated while hot with an excess of acetic acid. On cooling the arsonic acid separated as aggregates of microscopic needles in a yield of 7 g. When rapidly heated the substance darkens and softens at about 230–40° but does not melt entirely up to 265°. It is practically insoluble in boiling water or 50% alcohol.

Subs., 0.1322; 12.0 cc. N (26.0°, 757 mm) Subs., 0.3605; $Mg_2As_2O_7$, 0.1368.
Calc. for $C_{15}H_{16}O_6N_3As$: N, 10.26; As, 18.32. Found: N, 10.33; As, 18.32.

(B) Derivatives of Phenoxyacetyl-*p*-arsanilic Acid.

Phenoxyacetyl-arsanilic Acid, $C_6H_5OCH_2CONHC_6H_4AsO_3H_2(p\text{-})$.—4.4 g. of arsanilic acid were dissolved in 50 cc. of 20% sodium acetate solution and treated, while chilling and shaking, with 4 g. of phenoxyacetyl chloride. The reaction product separated at once. After making acid to congo red with hydrochloric acid the substance was filtered off, washed with water, and finally with ether. The yield was 3.5 g. Recrystallized from hot 50% alcohol, in which it is fairly readily soluble, the pure arsonic acid separates slowly as colorless, microscopic crystals which are soluble in boiling methyl alcohol or acetic acid, and very sparingly so in boiling water. It darkens slightly above 250° but does not decompose below 280°.

Subs., 0.3120; (Kjeldahl) 8 95 cc 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1370.
Calc. for $C_{14}H_{14}O_5NAs$: N, 3 99; As, 21.34. Found: N, 4 02; As, 21.19.

The acid was also prepared, although in poor yield, by boiling a solution of 3 g. of chloroacetyl-arsanilic acid[1] in 20 cc. of *N* aqueous sodium hydroxide with 1 g. of phenol under an air condenser for 1/2 hour. The substance was rapidly precipitated on cooling and adding acetic acid and was recrystallized from 50% alcohol. It separated slowly as wedge-shaped plates and prisms which showed the same properties as when made by the first method.

Subs., 0.2347; $Mg_2As_2O_7$, 0.1052.
Calc. for $C_{14}H_{14}O_5NAs$: As, 21.34. Found: 21.63.

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[1] THIS JOURNAL, **39,** 1456 (1917).

[1] *Ibid.*, **41,** 1810 (1919).

***p*-Oxamino-phenoxyacetyl-arsanilic Acid,** *p*-$HO_2CCONHC_6H_4OCH_2CONHC_6H_4AsO_3H_2$(*p*-).—In an attempt to prepare the amide of this acid by starting with *p*-hydroxy-oxanilamide, the conditions of the experiment caused the cleavage of the amide group with the formation of the carboxylic acid.

Equivalent amounts of chloroacetyl-arsanilic acid and *p*-hydroxyoxanilamide were dissolved separately in theoretical amounts of *N* sodium hydroxide solution and mixed, an immediate precipitation of the phenolic compound occurring. The mixture was boiled for 20 minutes, after which it reacted feebly acid, and the unchanged amide was filtered off and the filtrate acidified with hydrochloric acid. The resulting precipitate was dissolved in very dilute ammonia and the hot filtrate acidified with acetic acid. The cream-colored, microscopic crystals which separated proved to be the free carbonic acid formed by saponification of the amide in the boiling alkaline solution.

The substance darkens but does not melt below 280°. It is appreciably soluble in boiling water or 50% alcohol and separates from water with one molecule of water of crystallization.

Subs., air-dry, 0.4425; loss, 0.0196 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{16}H_{15}O_8N_2As.H_2O$: H_2O, 3.95. Found: 4.43.

Subs., anhydrous, 0.1610; 9.15 cc. N (23.5°, 753 mm.). Subs., 0.3577; $Mg_2As_2O_7$, 0.1293.

Calc. for $C_{16}H_{15}O_8N_2As$: N, 6.39; As, 17.10. Found: N, 6.48; As, 17.45.

***p*-Uramino-phenoxyacetyl-arsanilic Acid,** *p*-$H_2NCONHC_6H_4OCH_2CONHC_6H_4AsO_3H_2$(*p*-).—11.8 g. of chloroacetyl-arsanilic acid, 6.5 g. of *p*-hydroxyphenylurea, and 40 cc. of 2 *N* sodium hydroxide solution were refluxed for 1/2 hour. On cooling the *sodium salt* of the reaction product crystallized and the precipitation was completed by the addition of an equal volume of saturated sodium acetate solution. This salt was filtered off, washed with 20% sodium acetate solution, and finally with alcohol. For purification the crude product was dissolved in a small volume of water, treated with bone black, and then with alcohol until crystallization began. After filtration it was washed with 85% alcohol. The yield was 3.5 g., crystallizing as radiating masses of minute needles which contain approximately 3 molecules of water of crystallization.

Subs., air-dry, 0.5095; loss, 0.0531 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{15}H_{15}O_6N_3AsNa.3H_2O$: H_2O, 11.13. Found: 10.42.

Subs., anhydrous, 0.3510, (Kjeldahl) 23.5 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1240.

Calc. for $C_{15}H_{15}O_6N_3AsNa$: N, 9.75; As, 17.38. Found: N, 9.39; As, 17.05.

The free *arsonic acid* separates from the hot solution of the salt on adding acetic acid as aggregates of microscopic spindles which are practically insoluble in boiling water or 50% alcohol. It decomposes at about 280–3° with preliminary darkening.

Subs., 0.1332; 11.75 cc. N (29.0°, 765 mm.).

Calc. for $C_{15}H_{16}O_6N_3As$: N, 10.27. Found: 10.04.

o-Carboxamido-phenoxyacetyl-arsanilic Acid, o-$H_2NCOC_6H_4OCH_2CONHC_6H_4AsO_3H_2$(p-)—The reaction mixture from 11.2 g. of salicylamide was diluted to about 250 cc. and treated with sodium carbonate solution until just alkaline to litmus. The filtrate from the unchanged salicylamide was acidified with acetic acid, and on scratching the arsonic acid separated as fine needles. The crude acid was dissolved in a small volume of dil. sodium hydroxide and carefully neutralized with acetic acid. On adding an equal volume of saturated sodium acetate to the filtered solution the *sodium salt* quickly separated, forming a thick paste of crystals. The salt was washed with 20% sodium acetate solution and finally with alcohol and recrystallized from 85% alcohol, separating as prismatic needles containing approximately 5.5 molecules of water of crystallization.

Subs., air-dry, 0.5945; loss, 0.1177, *in vacuo* at 100° over H_2SO_4

Calc. for $C_{15}H_{14}O_6N_2AsNa$ $5.5H_2O$: H_2O, 19.23. Found: 19.79

Subs., anhydrous, 0.3026; (Kjeldahl) 14.5 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1120

Calc. for $C_{15}H_{14}O_6N_2AsNa$. N, 6.73; As, 18.02. Found N, 6.71; As, 17.87.

On acidifying a hot solution of the sodium salt with acetic acid the free *arsonic acid* separates as delicate needles which do not decompose below 280°. It is appreciably soluble in boiling 50% alcohol or acetic acid, but does not dissolve readily in the other hot solvents.

Subs., 0.2082; (Kjeldahl) 10.4 cc. 0.1 *N* HCl.

Calc. for $C_{15}H_{15}O_6N_2As$: N, 7.11. Found. 7.00.

p-Carboxamido-phenoxyacetyl-arsanilic Acid.—2.8 g. of p-hydroxybenzamide yielded, on cooling, a thick crystalline mass of the *sodium salt*. This was dissolved by dilution with warm water and the solution filtered from unchanged p-hydroxy-benzamide, after which the arsonic acid was precipitated as a colorless powder on acidification with acetic acid. This was reconverted into the sodium salt by dissolving in a small volume of dil. sodium hydroxide, carefully neutralizing with acetic acid, and salting out with saturated sodium acetate solution. The product so obtained was then recrystallized from a small volume of hot water, separating as rosets of long, flat, delicate needles which contained approximately 7.5 molecules of water of crystallization. The yield was 3.7 g.

Subs., air-dry, 0.4550; loss, 0.1097 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{15}H_{14}O_6N_2AsNa.7.5H_2O$: H_2O, 24.52. Found: 24.10.

Subs., anhydrous, 0.1547; 9.3 cc. N (27.0°, 758 mm.). Subs., 0.2994; $Mg_2As_2O_7$, 0.1117.

Calc. for $C_{15}H_{14}O_6N_2AsNa$: N, 6.73; As, 18.02. Found: N, 6.82; As, 18.00.

On adding acetic acid to a hot solution of the sodium salt the free *arsonic acid* separated slowly as long, glistening needles which do not melt below 280°, and are practically insoluble in the usual boiling solvents.

Subs., 0.1495; (Kjeldahl) 7.6 cc. 0.1 *N* HCl.

Calc. for $C_{15}H_{15}O_6N_2As$: N, 7.11. Found: 7.12.

NEW YORK, N. Y.

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, UNIVERSITY OF MINNESOTA.]

ORGANIC MERCURY COMPOUNDS DERIVED FROM *p*-BROMODIMETHYLANILINE.

BY FRANK C WHITMORE

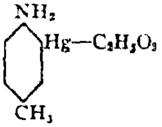
Received July 28 1919

The present paper is the first of a series in which the introduction of mercury in the *ortho* position to various substituted amino groups will be studied The work with the organic mercury compounds so obtained will deal especially with two fundamental reactions of organic mercury compounds in general These reactions may be represented by the single equilibrium equation

$$R_2Hg + HgX_2 \rightleftarrows 2RHgX$$

in which R represents any organic residue which has its free bond attached to carbon, and X represents any univalent acid radical The reaction normally runs to completion to the right because of the slight solubility of the organo mercuric salt RHgX in the organic solvents used The reaction may be reversed by using reagents which remove HgX_2 Such substances are alkaline reducing agents such as sodium stannite solution and compounds like potassium iodide and sodium thiosulfate which form mercuric complexes of considerable stability.

The introduction of mercury into a *para*-substituted aromatic amine has been studied only in the cases of *p*-toluidine and its dimethyl derivative[1] Klein mixed solutions of *p*-toluidine and mercuric chloride in ether and obtained crystals to which he assigned the formula $HgCl_2 2C_6H_4(CH_3)NH_2$. He obtained similar compounds with the bromide and the iodide of mercury. Pesci treated an alcoholic solution of *p* toluidine with an aqueous-alcoholic solution of mercuric acetate and obtained crystals of mercury (2-amino 5-methyl phenyl) acetate



This substance is insoluble in water but is readily soluble in organic solvents The corresponding hydroxide and chloride were made by treating it with conc aqueous potassium hydroxide and with alcoholic calcium chloride, respectively Pesci suggested that Klein's addition compound was really made up of one molecule of this chloride and one molecule of *p*-toluidine hydrochloride However he did not attempt to verify this conclusion by making Klein's compound from these substances. When the hydroxide was treated with a concentrated solution of sodium thiosulfate it was changed to mercury di-(2-amino-5-methyl phenyl).

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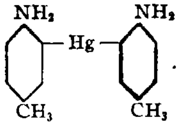
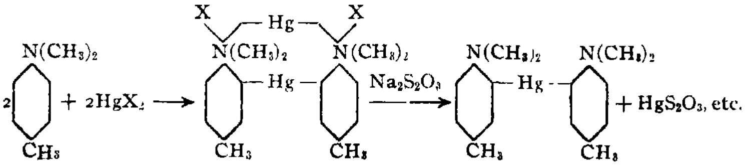
[1] Klein, *Ber*, 11, 744 (1878), 13, 835 (1880), Pesci, *Gazz chim ital*, 28, II, 101, 111, 460 (1898); *Z anorg. Chem.*, 17, 276, 281 (1898), Vecchiotti, *Gazz chim ital*, 48, II, 78 (1918).



Vecchiotti obtained the same results as did Pesci. Indeed the experimental data in the two papers are identical except in a few minor points.

Pesci treated dimethyl-*p*-toluidine with mercuric acetate and obtained mercury (2-dimethylamino-5-methyl phenyl) acetate from which he made the corresponding hydroxide, nitrate, chloride, bromide, and iodide. The hydroxide with sodium thiosulfate yielded the mercury diphenyl derivative, mercury di-(2-dimethylamino-5-methyl phenyl). Pesci briefly states that the acetate when treated with an excess of ammonium hydroxide gave the mercury diphenyl derivative.[1] He does not mention this reaction in the summary of his work published later.[2] This method of changing $RHgX$ to R_2Hg has apparently not been observed by any other worker with organic mercury compounds. Pesci proved the constitution of the mercury diphenyl derivative obtained from mercury (2-dimethylamino-5-methyl phenyl) hydroxide by synthesizing it from 3-bromo-dimethyl-*p*-toluidine and 1.5% sodium amalgam according to the method of Otto for making mercury diphenyl compounds.[3]

Pesci misinterpreted all of his reactions because he assigned incorrect structural formulas to all of his compounds except the mercury diphenyl derivatives. He believed that the salts which he had prepared each contained two benzene rings and two atoms of mercury in the molecule. He thought that one mercury was attached to two carbon atoms and the other was attached to two nitrogen atoms. The sodium thiosulfate was supposed to remove only the mercury attached to nitrogen. The difference between Pesci's views and the more modern one can best be shown by equations illustrating the formation of the acetate and the mercury diphenyl derivative.



Pesci's formulas.

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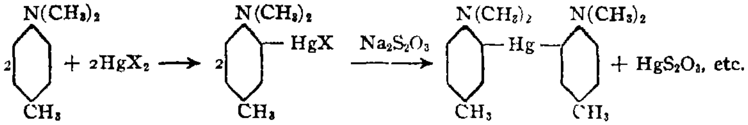
[1] *Gazz. chim. ital.*, **28**, II, 106 (1898).

[2] *Z. anorg. Chem.*, **17**, 176–281 (1898).

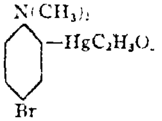
[3] Otto, *Ann.*, **154**, 94 (1870). This method was first developed by Frankland and was used by him in work in the aliphatic series *Ann.*, **130**, 105 (1864).



Modern formulas.

It will be seen that Pesci had the correct formulas for the mercury diphenyl compounds but did not correctly interpret their formation. Pesci's ideas were plausible enough when applied to the aromatic amines which he studied but they had to be discarded when Dimroth showed that "mercuration" is as general a reaction of aromatic compounds as sulfonation or nitration.[1] The best positive evidence that Pesci's double formulas are incorrect is that given Jacobs and Heidelberger who proved that the mercury compound obtained from aniline contains a primary amino group which can be diazotized and then coupled in the usual way with dimethylaniline or phenols.[2]

In the present investigation the starting point is *p*-bromo-dimethyl aniline. The dimethyl derivative was chosen as being likely to give fewer side reactions than any of the other substituted amines which are to be studied later. When an aqueous-alcoholic solution of mercuric acetate is allowed to stand with an alcoholic solution of *p*-bromo-dimethylaniline for several days there crystallizes out the organo-mercuric salt, mercury (2-dimethylamino-5-bromo-) acetate



The fine needle crystals of this substance are mixed with a certain amount of mercurous acetate. The mother liquor yields only tarry substances and more mercurous acetate. Thus at least two reactions are taking place, the introduction of the mercuri-acetate group into the ring and the oxidation of the *p*-bromo-dimethylaniline by the mercuric acetate. It was not found possible to eliminate this oxidation reaction completely. When *p*-bromo-diethylaniline is used instead of the dimethyl compound the oxidation becomes the chief reaction.[3] It was at first thought that the formation of mercurous acetate was due to a reducing action of the alcohol. This was disproved by the fact that boiling mercuric acetate for days with alcohol gave only minute traces of mercurous acetate. The use of more concentrated solutions of mercuric acetate with the *p*-bromo-dimethylaniline gave larger amounts of mercurous acetate. Heating the reaction mixture had a similar effect. To avoid a large concentration of mercuric acetate and thus to cut down its oxidizing action experiments were carried out in which the acetate was added very slowly and the mixture was stirred by a powerful mechanical stirrer. This did indeed cut down the amount of mercurous acetate formed but it also cut down the yield of the organo-mercuric salt.

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[1] *Z. anorg. Chem.*, **32**, 227ff (1902); **33**, 311ff (1903).

[2] *J. Biol. Chem.*, **20**, 513 (1915); *C. A.*, **9**, 1609 (1915).

[3] This reaction is being studied by Mr. A. R. Cade of this laboratory.

Various other salts were prepared from the acetate by treating the alcoholic solution of the latter with alcoholic solutions of suitable inorganic salts. In preparing the base alcoholic sodium hydroxide was used. The base was found useful in making salts which were not easily prepared by the precipitation method. This could be done by treating the base with the appropriate acid or better still with an ester of the acid. The formate was made in this way by heating the hydroxide with ethyl formate. This proved more convenient than the treatment of the hydroxide with formic acid or the treatment of the acetate with a formate solution. A slight excess of formic acid tends to remove some of the mercury from the ring while an excess of the ester does no harm. The purest sample of the acetate obtained was made from the hydroxide and ethyl acetate.

The change of the acetate or the hydroxide into the corresponding mercury diphenyl derivative, mercury di-(2-dimethylamino-5-bromo phenyl), was tried by all the usual methods. The reagents which bring about this change may be divided into two classes: The first class consists of alkaline reducing agents like sodium stannite solution. This reagent gave the mercury diphenyl derivative in 63% yield.

$$2R - Hg - X + 2NaOH + Na_2SnO_2 = R_2Hg + Na_2SnO_3 + 2NaX + H_2O + Hg.$$

The second class consists of those inorganic salts which form stable complex mercuric ions. Such substances are iodides, sulfides, and thiosulfates. Pesci usually employed the sulfides and thiosulfates in preparing his mercury diphenyl compounds. In the present research these substances gave very poor yields. Apparently the sulfide and thiosulfate of the organo-mercury base are more stable than those studied by Pesci and do not readily break up giving a molecule of an inorganic mercury compound according to the equation

$$(RHg)_2S + Na_2S = R_2Hg + Na_2HgS_2.$$

Potassium iodide proved to be the best reagent for preparing mercury di-(2-dimethylamino-5-bromo phenyl) as it gave a yield of 86% and a reaction mixture much easier to work up than did the sodium stannite which gave the next best yield.

$$2R - Hg - C_2H_3O_2 + 4KI = R_2Hg + 2KC_2H_3O_2 + K_2HgI_4.$$

It will be noted that all the products are water soluble except the desired substance.

If the theory that the formation of R_2Hg from RHgX depends on the removal of HgX_2 by the formation of a complex is true there should be a marked difference in the efficiency of iodides, bromides, and chlorides in bringing about this change. As is well known the iodide complex is by far the most stable and the chloride complex is the least stable. Experiments showed that while the iodide gave an 86% yield the bromide gave only a 3% yield and the chloride gave none of the mercury diphenyl compound. In the equation

$$2RHgX + 2MX = R_2Hg + M_2HgX_4$$

it will be seen that half of the mercury appears in an inorganic form which would give a precipitate with hydrogen sulfide. The filtrate from the reaction of sodium bromide with the organo-mercuric acetate gave an immediate black precipitate with hydrogen sulfide. The filtrate from the mixture of the acetate with a very large excess of alcoholic calcium chloride gave no precipitate with hydrogen sulfide, showing that no inorganic mercury compound had been formed.

It was thought that the organo-mercuric iodide might be changed to the mercury diphenyl derivative and mercuric iodide by long heating in a solvent in which the latter substance is much less soluble than the organic iodide. Such does not seem to be the case. Long boiling of a benzene solution of the organo-mercuric iodide gave no trace of mercuric iodide. Evidently the strong tendency for the formation of R-Hg-X depends not merely on the slight solubility of that type of substance but also on some peculiarity of the mercury atom which favors union with two groups at least as different as a hydrocarbon residue and an acid radical.

The formate was heated to see if it would yield the mercury diphenyl compound. The reduction did not stop at that point as almost all of the mercury appeared as metal and only a small amount of the mercury diphenyl compound was obtained. The chief organic product was *p*-bromodimethylaniline.

$$R—Hg—OCHO = Hg + RH + CO_2.$$

When the acetate was heated with zinc dust the products were mercury, zinc oxide, *p*-bromo-dimethylaniline, and unchanged acetate. Copper powder gave little action even on long boiling.

$$R—Hg—C_2H_3O_2 + Zn + H_2O = RH + ZnO + Hg + HC_2H_3O_2.$$

The acetic acid probably united with the large excess of alcohol present.

In all the reactions in which the mercury diphenyl compound was obtained after long boiling in an alcoholic solution small amounts of mercury metal were obtained. Usually this amounted to less than 0.1 g. The reaction which gives rise to this free mercury is evidently a very slow one as long boiling of the mercury di-(2-dimethylamino-5-bromo phenyl) with an excess of alcoholic potassium iodide or with alcohol alone only gave a very small amount of metallic mercury. Small amounts of *p*-bromo-dimethylaniline were sometimes obtained in these experiments. The reaction is possibly due to a slight reducing action of the alcohol on the organo-mercury compound.

The reaction of mercury di-(2-dimethylamino 5-bromo phenyl) with mercuric salts of monobasic inorganic acids was proved to proceed quantitatively according to the equation

$$R_2Hg + HgX_2 = 2R—Hg—X.$$

The reaction was carried out with mercuric chloride, bromide, iodide, and thiocyanate When mercuric salts of dibasic acids were used no satisfactory results were obtained Thus mercuric sulfate when heated with the mercury diphenyl compound gave mercuric oxide and *p*-bromo-dimethylaniline Probably the reaction proceeded as follows

$$HgSO_4 + C_2H_5OH = HgO + (C_2H_5)HSO_4$$

The ethylsulfuric acid would then react with the organic mercury compound liberating its mercury in inorganic form and leaving the *p*-bromo dimethylaniline The reaction of less easily hydrolyzable mercury salts of dibasic acids with mercury diphenyl and its derivatives will be studied later.

EXPERIMENTAL PART

Reaction of Mercuric Acetate with *p*-Bromo-dimethylaniline.

Reaction in Cold Dilute Solution.—80 g of 85% mercuric acetate was dissolved in 150 cc of hot water containing 5 cc of glacial acetic acid to prevent the hydrolysis of the acetate A small amount of mercurous acetate formed and was filtered off A solution of 40 g of *p* bromo-dimethylaniline in 700 cc of hot 95% alcohol was prepared and filtered into a one-quart fruit jar When both solutions had cooled to 30° the mercuric acetate solution was added to the solution in the fruit jar and the latter was stoppered tightly If the solutions were mixed at a higher temperature yellow mercuric oxide separated, as mercuric acetate reacts almost completely with hot alcohol undergoing "alcoholysis" No change was evident on mixing the cool solutions After standing at room temperature for about 6 hours long needle crystals began to form slowly. At the end of 6 days the formation of crystals had ceased After filtration by suction the crystalline residue (75 g) was heated under a reflux condenser for 15 minutes with 250 cc. of benzene, and then filtered through a steam funnel. The residue (7 5 g.) from this extraction on treatment with 100 cc. more of benzene gave no more soluble material. This residue insoluble in benzene was practically pure mercurous acetate. The benzene extract gave large amounts of pure white crystals as soon as it passed through the steam funnel. When thoroughly cold it formed a solid mass of crystals. Filtration left 62 g. of fine, pure white needles melting at

138 to 140°. 110 cc. of benzene was distilled off from the mother liquor and the residue was allowed to evaporate spontaneously giving 5.5 g. of crystals melting at 135°. The alcoholic mother liquor from the original reaction mixture gave no more crystals on long standing. 750 cc. of alcohol was distilled off On cooling a black tar was obtained which left 7.7 g. of mercurous acetate after extraction with hot alcohol. The alcoholic extract on standing gave 4.4 g. of an unmanageable black tar. In later preparations the mother liquor from the original reaction mixture was worked up only for the recovery of the alcohol. All the easily obtainable organo-mercuric acetate separated during the long standing. The evaporation of the mother liquor on the steam bath increased the oxidizing action of the mercuric acetate which resulted in the formation of mercurous acetate and the objectionable tar. Even without recovering any organic mercury compound from the original mother liquor, 40 g. of *p*-bromo-dimethylaniline gave 67.5 g. of mercury-(2-dimethylamino-5-bromo phenyl) acetate (74% yield)

Effect of Greater Concentration and Heating.--Two g. of *p*-bromo-dimethylaniline was heated with 10 cc. of alcohol and treated with a hot solution of 3.2 g. of mercuric acetate in 4 cc. of water and 2 cc. of glacial acetic acid. An oil separated at once. After heating for 5 minutes on the steam bath the oil disappeared and white, flaky crystals appeared. After heating for two hours the mixture was filtered. The white crystals proved to be mercurous acetate (1.2 g.). The alcoholic filtrate on evaporation gave a brown oil which did not crystallize even on standing for 3 months.

Effect of Slow Addition of the Mercuric Acetate with Vigorous Stirring.--77 g. of mercuric acetate was dissolved in 150 cc. of hot water containing 2 cc. of glacial acetic acid. The nearly clear solution was treated with 250 cc. of alcohol and filtered. 40 g. of *p*-bromo-dimethylaniline was dissolved in 500 cc. of alcohol and filtered into a large wide-mouth bottle provided with a powerful mechanical stirrer. The mercuric acetate solution was added in 10 cc. portions with constant stirring for 3 days. The crystals which had separated were treated in the usual way. The amount of mercurous acetate obtained from the first crystals was 4.2 g. as compared with 7.5 g. in a run in which all of the mercuric acetate, was added at once without stirring. However only 53.6 g. of the organo-mercuric acetate was obtained as compared with 67.5 g. in the other experiment.

Action of Mercuric Acetate with Alcohol.—Seven g. of mercuric acetate was treated with one cc. of acetic acid and 50 cc. of alcohol and heated until no more dissolved. About 0.1 g. of mercurous acetate was filtered off and the solution was heated under reflux for 5 days and nights. Filtration left less than 0.1 g. of mercurous acetate. Evaporation of the filtrate gave no more mercurous acetate.

Properties of Mercury 2-Dimethylamino-5-bromo Phenylacetate.

The acetate forms white, needle crystals melting at 144°.[1] It is almost insoluble in water and in petroleum ether (b. p. 35–45°). It is difficultly soluble in toluene, ethyl ether, and chloroform even on heating. It is fairly soluble in hot ethyl acetate, benzene, and carbon tetrachloride. It is very soluble in hot methyl alcohol, ethyl alcohol, and acetone. Carbon disulfide dissolves it readily even in the cold. The best crystals are obtained from methyl alcohol, ethyl alcohol, and benzene. Benzene is the best solvent for purification as it does not dissolve mercurous acetate, the impurity most likely to be present. The acetate is also soluble in cold conc. ammonium hydroxide.

Action of the Acetate with Hydrogen Sulfide.—A suspension of the organo-mercuric acetate in water gave no black precipitate with hydrogen sulfide. A small amount of a white, gelatinous precipitate formed showing that the sulfide of the mercury base is even less soluble than the acetate. An alcoholic solution of the acetate gave no black precipitate with hydrogen sulfide. A solution of the acetate in ammonium hydroxide was saturated with hydrogen sulfide and stoppered. The pure white precipitate which formed first had not changed at the end of 3 hours. At the end of 5 hours it had turned gray. These tests show that the mercury in mercury-(2-dimethylamino-5-bromo phenyl)-acetate is very completely "masked" or non-ionized. Similar experiments with the other organic mercury compounds prepared in this work showed that their mercury atoms were in the same masked condition.

Analysis of the Acetate for Bromine and for Mercury.—The organic mercury compounds mentioned in this paper were analyzed in the following way: A sample of the substance was decomposed in a Carius tube by means of fuming nitric acid. For complete decomposition heating at about 200° for at least 36 hours was required. In samples which were heated for shorter periods organic material was often left undecomposed. This apparently consisted of water-soluble nitro compounds which interfered with the quantitative precipitation of the mercury sulfide by ammonium sulfide. The contents of the Carius tube were diluted, transferred to a beaker, and nearly neutralized by sodium hydrogen carbonate free from halogen. Freshly prepared ammonium sulfide made from 10 cc. of conc. ammonium hydroxide was then added with stirring. The reaction mixture was allowed to stand on a steam bath overnight and was then filtered through a weighed Gooch crucible and dried at 110° for one hour. This method of analysis gave better results than the ordinarily recommended method of dissolving the mercury sulfide in sodium hydroxide and reprecipitating it with ammonium nitrate in order to get the precipitate in a more easily filterable form. By using the method indicated there was no trouble in filtering the precipitate. Moreover the mercury sulfide contained practically no free sulfur. This was shown by extracting the weighed precipitate for an hour with carbon disulfide. The loss in weight seldom exceeded 0.2 mg. The extraction with carbon disulfide was carried out in an extraction flask having a wide neck and provided with a reflux condenser. The Gooch crucible with a piece of filter paper tied around it was set in a support of heavy copper wire by means of a pair of long, straight tongs. A cone of filter paper was then placed on top of the crucible and the condenser was put in place. The purpose of the filter paper cone is to prevent the dropping of the condensed carbon disulfide from becoming rapid enough to wash the asbestos mat loose. Even with this precaution mercury sulfide might be washed through if the mat were unusually thin. In this case the outside filter paper will show the mercury sulfide and the analysis can be discarded. This happened only once in the analysis of the substances mentioned in this paper.

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[1] All melting points given in this paper are "uncorrected."

The filtrate and washing from the mercury sulfide, about 400 cc., were made barely acid with dil. nitric acid. In most cases no sulfur separated. When sulfur did appear it was usually from a sample which had not been thoroughly heated on the steam bath. The slightly acid solution was then warmed on the steam bath until no odor was perceptible, after which the clear solution was treated with silver nitrate and the silver halide was determined gravimetrically.

Calc. for $C_{10}H_{12}O_2NBrHg$. Hg, 43.7, Br, 17.5 Found Hg, 43.9, Br, 18.2.

Preparation of Other Salts from the Acetate.

The chloride, bromide, iodide, and thiocyanate were prepared by treating alcoholic solutions of the acetate with alcoholic solutions of calcium chloride, sodium bromide, potassium iodide, and potassium thiocyanate, respectively. In the cases of the chloride, bromide, and thiocyanate the product precipitated out of the hot solutions. As the iodide was much more soluble it was found desirable to mix the calculated amounts of the acetate and potassium iodide in a small volume of alcohol and reflux until most of the material had gone into solution. After filtering and cooling crystals separated which were freed from any potassium acetate by washing with a little water.

Properties of Mercury (2-Dimethylamino-5-bromo Phenyl) Chloride.--The chloride separated from alcohol or benzene in felted masses of very fine needles, m. p. 183°. Its solubilities are about the same as those of the acetate.

Subs., 0.3231 HgS, 0.1716, mixed AgBr + AgCl, 0.2498

Calc for $C_8H_9NClBrHg$ Hg, 46.0; Br + Cl (1:1), 26.6. Found: Hg, 45.8; Br + Cl, 26.9.

Properties of the Bromide.—The bromide tends to form larger crystals than the chloride and does not assume the "felted" appearance of the latter. M. p. 182°. It is rather more soluble in all the organic solvents than the chloride.

Calc. for C_8H_9NBrHg. Hg, 41.8. Found: 41.8.

Properties of the Iodide.—The appearance of the iodide is very much like that of the bromide. It is very much more soluble in organic solvents. M. p. 169°.

Calc. for $C_8H_9NBrIHg$: Hg, 38.0. Found: 37.8.

Properties of the Thiocyanate.—The thiocyanate separated from the reaction mixture in fine, white, gritty crystals, m. p. 135°, decomposing at 140°. It is insoluble in water and petroleum ether, slightly soluble in carbon tetrachloride, difficultly soluble in ether, soluble in acetic acid and carbon disulfide, very soluble on heating in methyl alcohol, ethyl alcohol, ethyl acetate, benzene, toluene, and chloroform. It dissolves readily in cold acetone. The only solvent which gives good crystals is ethyl acetate.

Calc. for $C_9H_9N_2BrSHg$: Hg, 43.8, Br, 17.5. Found: Hg, 43.4; Br, 17.4.

Preparation and Properties of the Base, Mercury (2-Dimethylamino-5-bromo Phenyl-)hydroxide.—An alcoholic solution of the acetate when treated with the calculated amount of sodium hydroxide in alcohol slowly deposited hard, wart-like masses of crystals. These melt at 162° and give off bubbles without blackening at 165°. No method was found for purifying this substance as it is practically insoluble in all solvents except acetic acid and ethyl acetate which, of course, change it back to the acetate. The powdered crystals were dried over soda lime and analyzed.

Calc. for $C_8H_{10}ONBrHg$: Hg, 48.1. Found: 48.4.

Preparation and Properties of the Formate.—Five g. of the hydroxide was heated under a reflux condenser with 50 cc. of ethyl formate for half an hour. Most of the hydroxide dissolved. When filtered and cooled the solution gave fine felted needles, m. p. 145°, decomposing at 150°. On standing the pure white crystals turned black, possibly due to the liberation of a small amount of mercury. The solubilities of the formate are similar to those of the acetate except that it is rather more soluble, notably so in water, chloroform, and carbon tetrachloride.

Calc for $C_9H_{10}O_2NBrHg$: Hg, 45.1; Br, 18.0. Found: Hg, 45.4; Br, 18.8.

Preparation of the Mercury Diphenyl Derivative. Mercury Di-(2-dimethylamino-5-bromo Phenyl).

27.6 g. of mercury(2-dimethylamino-5-bromo phenyl) acetate was mixed with 23 g. of powdered potassium iodide and heated with 200 cc of alcohol under a reflux condenser for 8 hours. At the end of the heating most of the material had dissolved giving a pale yellow solution. A small insoluble residue was colored dark by metallic mercury. After filtration the residue was extracted with cold benzene giving a solution which left 7.5 g. of crystals melting at 95 to 105°. The residue insoluble in benzene contained 0.5 g. of metallic mercury and a water-soluble inorganic compound (K_2HgI_4). The original yellow alcoholic solution deposited 8.2 g. of crystals melting at 114 to 119°. The mother liquor from these crystals was treated with 200 cc. of water and allowed to stand. 2.6 g. of crystals melting at 55° were obtained. This substance was proved to be *p*-bromo-dimethylaniline. The water-alcohol mother liquor gave no more solid even on evaporation. The yield of the mercury diphenyl derivative was 86%.

The 15.5 g. of crystals melting over 95° was dissolved in 30 cc. of hot benzene and mixed with 50 cc. of petroleum ether (b. p. 35 to 45°). The mixture was only slightly turbid. On standing, 12 g. of crystals melting 115° separated. Three more crystallizations raised the melting point to 123°. The mother liquors yielded a small amount of *p*-bromo-dimethylaniline.

Properties of the Diphenyl Derivative.—The substance crystallizes in fine, white needles, m. p. 123°. It dissolves in the same solvents as the acetate but to a much greater extent. It is readily soluble even in the cold in benzene, toluene, ether, carbon disulfide, and acetone.

Calc. for $C_{16}H_{18}N_2Br_2Hg$: Hg, 33.5; Br, 26.8. Found: Hg, 33.3; Br, 26.5.

Other Methods of Obtaining the Mercury Diphenyl Derivative.

Action of the Acetate with Ammonium Bromide.—9.2 g. of mercury-(2-dimethylamino-5-bromo phenyl) acetate was mixed with 4 g. of ammonium bromide and 200 cc. of alcohol and heated under a reflux condenser for 3 hours. The reaction mixture was worked up in the same way as that obtained by means of potassium iodide. The products obtained were 3.2 g. of the bromide, 0.2 g. of the mercury diphenyl compound, and 2.6 g. of *p*-bromo-dimethylaniline. The aqueous washings from the last substance contained large amounts of inorganic mercury compounds probably formed by the hydrobromic acid liberated by the dissociation of the ammonium bromide.

Action of the Acetate with Sodium Bromide.—The experiment was carried out in the same way as with the ammonium bromide. An insoluble residue consisted of 0.8 g. of metallic mercury and 6.4 g. of the bromide. The original solution deposited 1.2 g. of the bromide on cooling. Evaporation of the mother liquor left a sticky solid from which some inorganic mercury compound was extracted by water.

Action of the Acetate with Large Excess of Calcium Chloride.—2.3 g. of the acetate with 2 g. calcium chloride, and 25 cc. water and 100 cc. of alcohol were heated under a reflux condenser for 12 hours. The solid residue (0.8 g.) consisted of impure chloride (m. p. 171–4°). The solution on cooling deposited 1.1 g. of the chloride, m. p. 181°. Evaporation of the mother liquor gave 1.2 g. of solid, most of which dissolved in water. The water solution gave no action with hydrogen sulfide showing that *no inorganic mercury compound had been formed.*

Effect of Heat on the Iodide in Benzene Solution.—1.7 g. of the iodide in 50 cc. of benzene was heated under a reflux condenser for 6 hours. Only unchanged iodide was recovered. There was no evidence of the formation of any mercuric iodide or of metallic mercury.

Heating of the Mercury Diphenyl Compound with Excess of Potassium Iodide.—Long refluxing (15 hours) of the mercury diphenyl derivative with a large excess of potassium iodide in alcohol gave a very small amount (less than 0.1 g.) of metallic mercury and a very small amount of a water-soluble inorganic mercury compound. Most of the mercury diphenyl compound was recovered unchanged. When the mercury diphenyl derivative was refluxed with alcohol for 30 hours a slight amount of metallic mercury was formed. No inorganic mercury compound was obtained. Pure potassium mercuric iodide was refluxed for 10 hours with alcohol without the formation of any metallic mercury. These experiments show that the formation of metallic mercury is due to the action of the organo-mercury compounds with the alcohol. The reaction is in all cases a very slight one.

Action of the Acetate with Sodium Thiosulfate.—Five g. of the acetate in a mixture of 100 cc. of alcohol and 100 cc. of benzene was treated with 7 g. of sodium thiosulfate in 10 cc. of cold water. At first there was no change apparent on shaking. On standing the mixture turned black. An excess of conc. sodium thiosulfate solution was added. The black precipitate did not change. Filtration gave a clear solution which turned black on standing. The black substances were tarry and unmanageable. Probably they were mixtures of the organo-mercuric thiosulfate, the mercury diphenyl compound, metallic mercury, etc.

Action of the Acetate with Potassium Sulfide.—When an alcoholic solution of the acetate is treated with alcoholic potassium sulfide a pure, white precipitate forms at once. This almost instantly turns yellow, then gray, and finally black. This change is very rapid if the solutions are warm when mixed. Attempts were made to filter off the precipitate made from cold solutions before it had a chance to darken. These were unsuccessful as the sulfide is very gelatinous and filters slowly. During this slow filtration the precipitate always turned yellow. The white sulfide was finally obtained in the following way: 2.3 g. of the acetate dissolved in 250 cc. of cold alcohol was mixed with 20 cc. of alcohol containing 0.28 g. of potassium sulfide. The mixture was *immediately* poured into cold water. The precipitate remained white. It was filtered through a fluted filter paper and dried between several thicknesses of filter paper. When wet the sulfide formed a thick, gelatinous mass; when dry it formed hard, white flakes which turned slightly gray on long standing. When heated in a melting point tube it turned gray at about 97° and partly melted 115 to 120°. This behavior is probably due to the change of the sulfide into mercuric sulfide and the mercury diphenyl derivative (m. p. 123°). The sulfide was not soluble in any cold solvent. All hot solvents turned it gray except ether and petroleum ether in which it was not appreciably soluble. The other solvents dissolved part of it on heating but gave very tarry substances on evaporation. Evidently the decomposition of the organo-mercuric sulfide into mercuric sulfide and the mercury diphenyl derivative is not readily brought to completion.

Action of the Acetate and the Hydroxide with Stannous Compounds.—9.2 g. of the acetate in 400 cc. of alcohol treated with aqueous sodium stannite made from 2.3 g. of crystallized stannous chloride and an excess of sodium hydroxide gave 3.8 g. of the mercury diphenyl compound, a 63% yield.

When the hydroxide was refluxed in alcohol with stannous chloride the chief products were the organo-mercuric chloride, metallic mercury and *p*-bromo-dimethylaniline. The formation of the last named substance was probably due to hydrochloric acid liberated by the hydrolysis of the stannous chloride.

When the base was treated with freshly precipitated stannous hydroxide suspended in alcohol only a very small amount of the mercury diphenyl compound was obtained. This was probably due to the slight solubility of both substances in alcohol.

Effect of Heat on the Formate.—One g. of the formate was heated for 30 hours with 20 cc. of benzene and 20 cc. of alcohol. 0.4 g. of metallic mercury was formed. The filtrate on standing gave less than 0.1 g. of the mercury diphenyl compound and about 0.5 g. of *p*-bromo dimethylaniline.

Action of the Acetate with Zinc Dust.—4.6 g. of the acetate mixed with 0.4 g. of zinc dust and 100 cc. of alcohol was heated under a reflux condenser for 2 hours. The residue weighed 0.9 g. and consisted of metallic mercury and some zinc oxide (or hydroxide). The solution gave 1.3 g. of unchanged acetate and 0.9 g. *p*-bromo-dimethylaniline. When the experiment was repeated, using copper powder, no product but the original acetate and a very small amount of metallic mercury was obtained.

Action of Mercuric Salts with the Mercury Diphenyl Derivative, Mercury Di-(2-dimethylamino-5-bromo Phenyl).

One g. of the mercury diphenyl compound mixed with 0.5 g. of mercuric chloride and 50 cc. of alcohol and refluxed for 4 hours gave 1.5 g. of the chloride, melting at 181°. Yield, 100%.

A similar experiment using mercuric bromide gave 1.5 g. of the bromide, melting at 179°. Yield, 94%.

Using mercuric iodide instead of the chloride, 1.7 g. of the iodide was obtained, melting at 160°. Yield, 95%. It will be noted that the iodide obtained in this way is not as nearly pure as are the corresponding bromide and chloride.

When mercuric thiocyanate was used in place of the halides the organo-mercuric thiocyanate melting at 130° was obtained in 87% yield.

One g. of the mercury diphenyl compound refluxed with 0.5 g. of mercuric sulfate in alcohol gave a yellow solid which proved to be basic mercuric sulfate and a small amount of *p*-bromo-dimethylaniline.

Summary.

1. Mercuric acetate reacts with *p*-bromo-dimethylaniline introducing the mercuri-acetate group, —Hg—O—CO—CH_3, into the *ortho* position. Yield, 74%.

2. The mercury-(2-dimethylamino-5-bromo phenyl-) acetate obtained in this way readily yields other salts by double decomposition reactions. The chloride, bromide, iodide, and thiocyanate were prepared and their properties studied.

3. The organo-mercuric hydroxide of this series was prepared. From it was made the corresponding formate by treatment with ethyl formate. This treatment of an organo-mercuric hydroxide with an ester gives a new method for making organo-mercuric salts which cannot conveniently be made in any other way.

4. The mercury diphenyl derivative was made and its properties studied.

5. The change of compounds of the type R—Hg—X to those of the mercury diphenyl type, R_2Hg, may be brought about by alkaline reducing agents and by substances like iodides, sulfides, and thiosulfates It is suggested that this reaction depends upon the ability of these substances to form very stable complex ions of mercury. In confirmation of this it has been found that the iodides are most efficient of the halides in bringing about this reaction. Bromides bring it about to only a very slight extent and chlorides do not do so at all.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY, No. 325.]

THE PROTEOLYTIC ACTIVITY OF PANCREATIC AMYLASE PREPARATIONS.

BY H. C. SHERMAN AND DORA E. NEUN.

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Previous papers from this laboratory[1] have described the purification and properties of pancreatic amylase preparations which, while not chemically pure, appear to constitute a definite product of protein nature, similar in most of its chemical characteristics to the malt amylase described by Osborne.[2] but showing much greater enzymic activity. Several years' study leads us to conclude in regard to our pancreatic amylase as did Osborne in his study of the amylase of malt that the protein of which the final preparation is composed is not merely a carrier, but probably more nearly represents an approximate isolation of the enzyme itself, though as we have pointed out elsewhere,[3] there is reason to believe that in each case a part of the enzyme may have undergone. during its purification, some hydrolysis or chemical rearrangement with a corresponding diminution of amylolytic power.

Last year we showed in some detail[4] that the purified pancreatic amylase preparations made in this laboratory exhibit also a proteolytic activity similar to that of trypsin, and fully equal in intensity to that of the best commercial trypsins which we have tested, though they are not so active proteolytically as another of our preparations from the pancreas.

The marked proteolytic activity of our purified pancreatic amylase preparation is characteristic of it, as contrasted with our purified amylase preparations from malt and from *Aspergillus oryzae*. It is well known that extracts of malt and of *Aspergillus oryzae* contain proteases, as do also commerical taka-diastase and crude precipitated malt diastase; but the purified malt amylase prepared as described in a previous paper[5] has now been tested throughout a wide range of hydrogen ion concentration without revealing any proteolytic action, and the amylase preparation from *Aspergillus oryzae*, in such degree of purity as has so far been obtained, shows only about one-fortieth of the proteolytic activity of the purified pancreatic amylase preparation.

The proteolytic activity thus shown by the pancreatic amylase preparation might be attributed to the presence in the pancreas of a protease independent of the amylase but having so nearly the same solubilities as to remain admixed with the amylase throughout the purification process to which the latter has been subjected. Possibly a part of the trypsin may thus accompany the amylase.

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[1] Sherman and Schlesinger, THIS JOURNAL, 33, 1195 (1911); 34, 1104 (1912); 37, 1305 (1915).

[2] Osborne, *Ibid.*, 17, 587 (1895); *Ibid.*, 18, 536 (1896).

[3] Sherman and Schlesinger, *Ibid.*, 37, 1305 (1915).

[4] Sherman and Neun, *Ibid.*, 40, 1138 (1918).

[5] Sherman and Schlesinger, *Ibid.*, 37, 643 (1915).

The facts observed and to be described below also suggest the possibility that the amylolytic and proteolytic activities may in this case be the characteristic properties of interrelated substances or may conceivably be two properties of the same substance, analogous to the finding of Osborne and Wells[1] that a single isolated protein (hordein or gliadin) may contain more than one antigenic radical. One is also reminded of the problem of the possible identity of pepsin and rennin.

The experiments described below were undertaken with a view to throwing some further light upon the nature of the relationship which exists between the amylolytic and proteolytic activities of our purified pancreatic amylase preparations.

Experimental.

In our usual method of purification,[2] high grade commercial pancreatin is extracted with 50% alcohol, this filtrate is precipitated with alcohol-ether mixture and the precipitate dissolved in water and precipitated with absolute alcohol, then dissolved and dialyzed in 50% alcohol containing maltose to retard deterioration, and finally precipitated with an equal volume of 1 : 1 alcohol-ether mixture. In this procedure there settles out in the dialyzing sacs some material which, originally soluble in 50% alcohol, has now become insoluble in the same solvent apparently as a result of the preceding precipitation with absolute alcohol or standing in 50% alcohol, or both. This product, "sac precipitate," has little, if any, diastatic power, but has higher proteolytic activity than has the final amylase preparation. In fact, it is much the most active protease of which we have knowledge.

In order to test whether the amylase and protease activities of the final product of our usual method of purification are due to admixed substances which can be separated by differing solubilities in alcohol, we substituted for the usual final precipitation with 1 : 1 alcohol-ether, a precipitation with an equal volume of a mixture of two parts alcohol to one of ether, the product thus obtained being called Precipitate A, after which a second precipitate, B, was obtained by adding more ether. Precipitate A was separated by centrifugal force, with the additional precaution of cooling the centrifuge with liquid air,[3] and decantation; Precipitate B, by filtration after the addition to the solution decanted from Precipitate A, of an amount of ether equal to half its volume.

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[1] Osborne and Wells, *J. Infec. Diseases*, 12, 341 (1913)

[2] Sherman and Schlesinger, This Journal, 37, 1305 (1915).

[3] This precaution appeared important because otherwise there was a large loss of amylolytic power in the precipitation and handling of the final products

Typically the amylolytic activity of Precipitate A was lower than that of Precipitate B; but the latter was not more active than our usual amylase preparations.

The proteolytic activity was higher in Precipitate A than in Precipitate B.

The full description of a single typical experiment follows:

Preparation 78 (N. 14):—20 g. of air-dry pancreatin was mixed with 200 cc. of 50% alcohol at 5° and allowed to stand 20 minutes surrounded by a freezing mixture, then filtered, and the filtrate received in cylinders surrounded by a freezing mixture. The residue was washed with absolute alcohol and ether, then dried in a vacuum desiccator. (The washings were kept separate from the filtrate and were rejected.) The filtrate or 50% alcohol extract, which amounted to 142 cc. was poured into one liter of alcohol-ether mixture (1:4) and after standing 20 minutes surrounded by a freezing mixture, the supernatant liquid was decanted and the residue was dissolved in 57 cc. of triply distilled water at 1° and this solution was poured into 430 cc. of absolute alcohol which had been chilled in a freezing mixture. The resulting flocculent precipitate was made to settle by centrifuging for 15 minutes, liquid air being continuously introduced into the centrifuge to keep it cold. The temperature of the liquid was thus kept below 14° even after continuous centrifuging for 15 minutes. The precipitate was dissolved in 250 cc. of 50% alcohol containing 5 g. of maltose and dialyzed in two collodion sacs against 2 liters of cold 50% alcohol for 40 hours, changing the dialysate morning and evening. The 3 dialysates were rejected. The precipitate which appeared in the dialyzing sac was filtered in an ice chest, the filtrate[1] being received in cylinders packed in a freezing mixture. This filtrate (330 cc.) was mixed with an equal volume of alcohol-ether mixture (2:1) and the resulting flocculent precipitate was collected by centrifuging for 15 minutes with a continuous stream of liquid air passing into the centrifuge as described above. (In this case a maximum temperature of 19° was reached.) The precipitate thus obtained was scraped out of the centrifuge cups, dried *in vacuo* and weighed as "Precipitate A." The filtrate was poured into half its volume of ether, the resulting precipitate separated by filtration at ice box temperature, dried *in vacuo*, and weighed as "Precipitate B."

The weights and activities of these products are shown in Table IV.

Amylolytic Activity.—To permit of comparison with other preparations, the amylolytic activities of the 4 fractions obtained in each of several experiments are given in Table I, both in terms of the "new scale" diastatic powers as generally used in this laboratory since 1910, and as "saccharogenic powers" defined as the number of mg. of maltose formed per hour at 40° by each mg. of enzyme acting upon a sufficient excess of substrate.

As was to be expected in view of earlier work the extractions, dialyses and precipitations with alcohol necessarily involve more or less destruction or inactivation of the amylase (probably at least half of that present), which together with experimental errors, make the results somewhat irregular when the activities of the different fractions are stated in quantitative terms. The general trend of the results is, however, quite pronounced and uniform. The residue from extraction with 50% alcohol has much less amylolytic power than the original pancreatin, while that of the "sac precipitate" is much smaller still, negligible, in fact, as compared with the activity of the material which remains to be precipitated by alcohol. The amylase activities of the two alcohol precipitates (A and B) are of the same order of magnitude both with each other and with the final products of the method of purification which we have usually employed in the past. Typically, as in Preparation 78 (N. 14), the amylolytic power of Precipitate B is higher than that of Precipitate A. It is, however, not higher than has been obtained by the method of purification previously employed.

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[1] The precipitate was subsequently washed 3 times with cold 50% alcohol by centrifuging and decantation, the washings rejected and the washed precipitate dried *in vacuo*.

TABLE I—AMYLOLYTIC ACTIVITIES OF PANCREAS PRODUCTS

Preparation number	Residue	Sac precipitate	Precipitate A	Precipitate B
	Diastatic powers "new scale of 1910"			
72 (N 8)	65	20	2394	3000
75 (N.11)	82	51	1955	2195
77 (N 13)	133	23	2677	2500
78 (N.14)	152	51	2624	3700
81 (N 17)	81	49	2022	2800
	Saccharogenic powers			
72	330	110	11580	14280
75	410	256	9550	10500
77	680	110	12800	10150
78	756	256	12600	17370
81	410	250	13900	13400

Proteolytic Activity.—If we express proteolytic activity in terms of the number of parts of casein nitrogen converted, (*a*) to soluble products, or (*b*) to amino nitrogen, by one part of enzyme preparation per hour at 40°, then the data for the proteolytic activities of the fractions obtained in typical experiments are as shown in Table II.

TABLE II—PROTEOLYTIC ACTIVITIES OF PANCREAS PRODUCTS.

Preparation number	Residue.	Sac precipitate	Precipitate A	Precipitate B.
	Nitrogen digested to soluble forms (*a*)			
72	12	256	80	55
75	12	256	89	63
77	13	257	90	55
78	13	252	83	68
81	12	214	94	69
	Nitrogen digested to amino form (*b*)			
72	1.3	26.4	7.3	5.5
75	1.3	29.6	12.5	5.7
77	1.4	28.6	8.8	5.7
78	1.4	31.2	11.5	6.2
81	1.1	25.8	8.6	5.4

It will be seen that the sac precipitates have much higher proteolytic activities than either of the later alcohol precipitates, A or B. As between the latter, Precipitate A always exceeds Precipitate B in proteolytic activity. These relations hold uniformly true whether the proteolytic activity be judged from the total "soluble" nitrogen or the amino nitrogen of the cleavage products of the casein. In order to make the proteolytic powers comparable with the amylolytic (saccharogenic) powers, they are best expressed in terms of protein digested per hour by unit quantity of enzyme preparation. The data *(a)* of Table II then become as shown in Table III.

TABLE III.—PROTEOLYTIC ACTIVITIES IN TERMS OF CASEIN DIGESTED TO SOLUBLE PRODUCTS

Preparation number	Residue	Sac precipitate	Precipitate A	Precipitate B
72	75	1600	500	344
75	75	1600	550	394
77	81	1607	563	344
78	81	1575	519	425
81	75	1338	588	431

Of the total enzymic activity of the pancreatin powder employed in such experiments a larger proportion of the proteolytic than of the amylolytic power is recovered in the 4 products here described. This is shown in quantitative terms in Table IV.

Discussion.—The exceedingly unstable nature of the material under purification, the relatively large losses which appear to be unavoidably involved in precipitation and reprecipitation if the characteristic amylolytic activity is not to be destroyed in the process, the dependence of the yields of precipitate upon minute details of manipulation which probably cannot be completely formulated and standardized until our knowledge of the behavior of colloidal substances is further developed, are all conditions which tend against closely concordant results in successive experiments, even after long practice has acquainted one with the many sources of difficulty and with the necessity for the utmost care and caution at every step.

For the same reasons and particularly because of the great tendency to loss of amylolytic activity when pancreatic amylase in the absence of salts and carbohydrates is held in solution or subjected to precipitation, it was not feasible to push the fractionation further by repeatedly dissolving and reprecipitating as would have been done in a similar study of a simpler or more stable substance. This deterioration in activity of the enzyme in solution which has been emphasized and discussed in previous papers and is much more pronounced in the case of amylolytic than of proteolytic action might of itself explain the fact that of the total enzyme activity of the original pancreatin employed in the experiments referred to in Table IV, about 3 times as large a proportion of the proteolytic as of the amylolytic activity was recovered.

TABLE IV—YIELDS OF AMYLASE AND PROTEASE IN FRACTIONATION

Description	Weight G	Amylase "Power" of preparation	Amylase Units of activity	Amylase Per cent of original total	Protease "Power" of preparation	Protease Units of activity	Protease Per cent of original total
Pancreatin 7	20 000	1795	35900	100 00	82	1640	100 00
Preparation 72							
Residue	10 515	329	3459	9 64	75	789	48 11
Sac ppt	0 140	117	16	0 04	1600	224	13 66
Ppt A	0 042	11580	486	1 35	500	21	1 28
Ppt B	0 062	14275	885	2 47	344	21	1 28
				13 50			64 33
Preparation 75							
Residue	10 175	410	4172	11 62	75	763	46 52
Sac ppt	0 187	260	49	0 14	1600	299	18 23
Ppt A	0 126	9550	1203	3 35	556	69	4 20
Ppt B	0 159	10500	1670	4 65	394	61	3 72
				19 76			72 67
Preparation 77							
Residue	8 906	686	6110	17 02	81	721	43 96
Sac ppt	0 237	114	27	0 08	1607	381	23 23
Ppt A	0 076	12820	974	2 71	563	43	2 62
Ppt B	0 171	10130	1732	4 82	344	59	3 60
				24 63			73 41
Preparation 78							
Residue	9 226	756	6972	19 42	81	748	45 60
Sac ppt	0 151	256	39	0 11	1575	238	14 51
Ppt A	0 044	12600	555	1 55	519	23	1 40
Ppt B	0 139	17370	2414	6 73	425	59	3 60
				27 81			65 11
Preparation 81							
Residue	9 864	409	4034	11 24	75	740	45 12
Sac ppt	0 203	246	50	0 14	1339	272	16 59
Ppt A	0 077	13920	1072	2 98	588	45	2 74
Ppt. B .. .	0 284	13390	3803	10 59	431	122	7 44
				24 95			71 89

The following notes on data of individual experiments may also be considered at this point

Preparation 78 (N 14) has been described as typical since we regard it as the most representative in details of method and in results In the tables, however, are also included the data of 4 other experiments, each of which shows some appreciable difference from No 78 either in the yield or activity of one or more of the products obtained The principal differences of each of these from No 78 may be briefly noted.

In No 72 the amylolytic activity of the residue was less well conserved and the yield of Precipitate B was much lower. Moreover, a higher temperature was reached during centrifugation than in the case of No. 78, hence the percentage of original enzyme activity recovered in the 4 products was somewhat lower for proteolytic and much lower for amylolytic power.

In No. 75 the final alcoholic Precipitates A and B, especially the latter, suffered great loss of amylolytic power because of insufficient control of temperature, especially during centrifugation. The larger yields resulted in a relatively high total recovery of proteolytic activity.

In No. 77 the weight of the "sac precipitate" and Precipitate A are higher and their powers are normal, while the weight of Precipitate B is also higher (than in Preparation 78) but its enzymic activity, both amylolytic and proteolytic, is low. The sum of the 4 fractions shows lower amylolytic and higher proteolytic power than in Preparation 78.

In No. 81 there appears to have been a better extraction of amylase from the pancreatin at the beginning of the process and hence a larger yield of each of the 3 precipitates obtained later It appears, however, from their amylolytic powers, that Precipitates A and B are not as well separated from each other as in Preparation 78 and also that in the present experiment Precipitate B has either suffered a deterioration of amylolytic power or is contaminated with inert material as in No. 77, or both.

Since the sum of either the weights or the units of amylase or of protease action of the 4 fractions here prepared from pancreatin is much below the total of the pancreatin powder which served as starting material, there is evident need of caution in quantitative interpretation of the results. It is, however, apparent from the data tabulated above that the purification process results in a marked concentration of amylolytic power in the final Precipitates A and B. Thus, in Preparation 78, Precipitate A has about seven times, and Precipitate B about 10 times the amylolytic activity of the original pancreatin. Proteolytic activity is concentrated to a much greater extent in the "sac precipitate," and to a lesser but considerable extent in the final Precipitates A and B.

Special interest attaches to the comparison of the amylase and protease activities of the Precipitates A and B with each other and with our usual amylase preparations. In the case of a typical fractionation experiment such as that described above as Preparation 78, the high proteolytic activity of Precipitate A obviously suggests that our usual amylase preparation may be a mixture of amylase and protease, of which the protease is here concentrated in the first precipitate. In this case Precipitate B should have shown a higher concentration of amylase than our usual amylase preparations, except that because of the added manipulation a greater deterioration of amylase was necessarily involved.

On the whole, it seems probable that a partial separation of a mixture of amylase and protease was accomplished but that amylolytic activity was partially lost because of the extra manipulation, since amylolytic activity deteriorates much more rapidly than proteolytic, at least under conditions such as obtained in these experiments.

The further possibility that there are enzyme particles, which have both amylolytic and proteolytic activities is not excluded. Both possibilities should be taken into account in future consideration of the problem of specificity of enzyme action.

We are greatly indebted to the Carnegie Institution of Washington for grants in aid of this investigation.

NEW YORK, N. Y.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF NORTH CAROLINA.]

THE ACTION OF BASIC REAGENTS ON SCHIFF'S BASES. I. THE CHLORALNITRANILINE GROUP.

BY A. S. WHEELER AND S. C. SMITH

Received August 23, 1919

Theoretically a great many compounds are included under the designation of Schiff's Bases, since it comprehends all condensation products of primary aromatic amines with aldehydes and ketones of every description. Actually a considerable number of Schiff's Bases have been described, beginning with the first mention of such products by Laurent and Gerhardt,[1] who condensed aniline with benzaldehyde. But H. Schiff[2] made the first real study of the reaction, condensing a humber of amines and aldehydes. The reaction is indicated by the equation:

$$R.CHO + 2R.NH_2 = R.CH(NHR)_2 + H_2O.$$

These bases are stable, as a rule though a small number are sensitive to light and may be decomposed readily by hot water. Among these are compounds of the *meta* series and certain naphthylamine derivatives. The investigations of Schiff's Bases in the organic laboratory of the University of North Carolina have dealt only with three aldehydes, chloral, vanillin and piperonal, but with a wide variety of amines.

It has been noted generally by observers that Schiff's Bases are sensitive to acids, being resolved into their constituents by strong hydrochloric acid. Their behavior toward basic reagents however has been quite generally overlooked. Wallach[3] noted that the condensation product of aniline and chloral was slowly decomposed by aqueous potash but rapidly by alcoholic potash, giving aniline, chloroform and phenylisocyanide. The presence of the two latter substances indicate that the decomposition takes place in 3 stages. This uninteresting behavior with alcoholic potash undoubtedly caused later investigators of Schiff's Bases to pass by this reaction. One of us[4] observed that the condensation product of chloral and *p*-nitraniline was changed immediately by alcoholic potash from a yellow substance to a brilliant red one. Upon puri-

[1] *Compt. rend.*, 30, 404 (1850).

[2] *Ann. Chem. Pharm.*, 131, 118 (1864).

[3] *Ann.*, 173, 278 (1874).

[4] Wheeler and Glenn, *J. Elisha Mitchell Sci. Soc.*, 19, 63 (1903).

fying the product, however, a yellow compound was obtained in which one chlorine atom was replaced by the hydroxyl group

$$CCl_3CH(NHNO_2C_6H_4)_2 + KOH = CCl_2OH.CH(NHNO_2C_6H_4)_2 + KCl.$$

The red compound appeared to be an intermediate product for it disappeared when the reaction mixture was poured into water. It was then found that sodium methylate reacted similarly, replacing one chlorine atom by the methoxy group. In all of the reactions with the *o*- and *p*-nitraniline condensation products a brilliant red substance appeared only to disappear in the presence of water. All of the products are of a rich yellow color. We now find that sodium ethylate has a similar action and also that the *o*-nitraniline condensation product acts analogously to the *para* compound. The method of preparation of Wheeler and Glenn has been decidedly improved by dissolving or suspending the amines in acetone instead of alcohol. The reaction is almost immediate, the quality of the product is much better and the yield is much increased.

Although the *o*- and *p*-nitraniline condensation products of chloral readily yield these stable derivatives, the *m*-nitraniline product was found to be very sensitive to basic reagents. It is resolved at once in the cold into its constituents. The behavior then of Schiff's Bases toward basic reagents depends upon the nature of the substituents in the benzene ring of the amine and also upon whether it is a *meta* compound or not.

Experimental Part.

I. Behavior of *N*,*N'*-β,β,β-trichloroethylidene-bis-*o*-nitraniline.

***N*,*N'*-β,β,β-Dichlorohydroxyethylidene-bis-*o*-nitraniline**, $CCl_2OHCH(NHNO_2C_6H_4)_2$.—The trichloro compound was prepared according to the directions of Wheeler and Weller.[1] Its reaction with alcoholic potash was tested by allowing a mixture to stand 36 hours. A brown flocculent precipitate of indefinite melting point settled out. Another mixture was warmed a few moments and poured into 4 volumes of water. A yellow substance which melted at 142° after several recrystallizations was obtained but the yield was only 40%. The following plan was finally adopted: Five g. of the trichloro compound was suspended in 25 cc. of acetone and 15 cc. of a 10% alcoholic potash solution was added. The mixture became dark red immediately. It was warmed until it began to boil and was at once poured into 5 volumes of ice-water. After standing a few hours to insure full crystallization the precipitate was filtered off. The yield was 4.4 g. or about 91% of the theoretical amount. The crude product melted at 139–140° but upon recrystallization from alcohol the melting point was raised to 143°.

Subs., 0.1582; AgCl, 0 1186.

Calc. for $C_{14}H_{12}O_5N_4Cl_2$: Cl, 18.37. Found: 18.52.

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[1] This Journal, 24, 1063 (1902).

The pure compound is brilliant yellow, crystallizing from alcohol in prisms, m. p. 143°. It is soluble in about 30 parts of hot alcohol and 120 parts of cold alcohol. It is very soluble in acetone and in chloroform, slightly soluble in ligroin and insoluble in water. It turns red with alcoholic potash. Strong acids decompose it. If heated with conc. hydrochloric acid, it dissolves, and a precipitate then forms which again dissolves. On pouring this solution into water, *o*-nitraniline crystallizes out.

***N*,*N'*-β,β,β-Dichloromethoxyethylidene-bis-*o*-nitraniline,** CCl_2OCH_3-$CH(NHNO_2C_6H_4)_2$.—Two g. of the trichloro compound was suspended in 20 cc. of acetone and to this was added 10 cc. of a sodium methylate solution containing 5 g. of sodium per 60 cc. of methyl alcohol. The mixture became dark at once. It was heated to boiling and at once poured into 4 volumes of ice water. The yellow precipitate weighed 1.75 g. or 89% of the theoretical amount. The crude substance melted at 140° but after several recrystallizations from alcohol the melting point was raised to 147°.

Subs., 0.2874, AgCl, 0.2049

Calc. for $C_{15}H_{14}O_5N_4Cl_2$ Cl, 17.69 Found 17.60

The pure substance is bright yellow, crystallizing from alcohol in rectangular plates, m. p. 147°. It is soluble in about 25 parts of boiling alcohol and 100 parts of cold alcohol. It turns dark red with alcoholic potash. With hot aqueous potash the red color finally becomes purple.

***N*,*N'*-β,β,β-Dichloroethoxyethylidene-bis-*o*-nitraniline,** $CCl_2OC_2H_5$-$CH(NHNO_2C_6H_4)_2$.—The reaction of sodium ethylate upon the trichloro compound was carried out as with sodium methylate. The crude precipitate weighed 1.8 g. or 88% of the theoretical amount. It melted at 132° but on recrystallizing from alcohol the melting point was raised to 135°.

Subs., 0.2846; AgCl, 0.2000

Calc. for $C_{16}H_{16}O_5N_4Cl_2$: Cl, 17.13. Found: 17.38

The pure substance is a very brilliant, yellow compound, crystallizing from alcohol in rectangular plates, m. p. 135°. It is soluble in about 50 parts of boiling alcohol and 100 parts of cold alcohol. Its behavior is analogous to that of the methoxy compound.

II. Behavior of *N*,*N'*-β,β,β-Trichloroethylidene-bis-*m*-nitraniline.

No derivatives of the *meta* compound could be obtained with alcoholic potash, sodium methylate or sodium ethylate. In no case was a red coloration produced. The precipitate obtained on pouring the reaction mixture into water consisted of *m*-nitraniline. The decomposition was immediate and took place in the cold.

III. Behavior of *N*,*N'*-β,β,β-Trichloroethylidene-bis-*p*-nitraniline.

The derivatives of this compound with alcoholic potash and sodium methylate were described by Wheeler and Glenn. Their method was improved by suspending the trichloro compound in acetone, but a little longer heating was required than with the *ortho* compound. The yield was increased to 78% of the theoretical amount for the hydroxy derivative and to 87% for the methoxy compound. These compounds are described in the *Review of American Chemical Research*, **9**, 559 (1903) as "Derivatives of Trichloroethylidenedi-*p*-nitrophenamine." But the nomenclature is changed in this paper to conform to the plan adopted in the Decennial Index of *Chemical Abstracts*. The ethoxy compound described below is new.

N,*N'*-β,β,β-**Dichloroethoxyethylidene-bis-*p*-nitraniline,** $CCl_2OC_2H_5$-$CH(NHNO_2C_6H_4)_2$.—Five g. of the trichloro compound was suspended in 75 cc. of acetone and 25 cc. of sodium ethylate solution (5 g. of sodium per 60 cc. of ethyl alcohol) was added. The deep red mixture was heated on the steam bath for 10 minutes and then poured into 5 volumes of ice-water. The precipitate weighed 4.5 g. or 88% of the theoretical amount. It melted at 140° but after purifying by alcohol at 147°.

Subs., 0.2149, AgCl, 0.1491

Calc. for $C_{16}H_{16}O_5N_4Cl_2$: Cl, 17.13. Found: 17.12

The pure substance is bright yellow, crystallizing from alcohol in fan-shaped crystals, m. p. 147°. It gives a deep red color with alcoholic potash and the alcoholates. Heated with aqueous potash a green color is obtained instead of a purple. Heated with conc. hydrochloric acid it yields *p*-nitraniline hydrochloride.

Summary.

1. Schiff's Bases obtained by condensing *o*- and *p*-nitraniline with chloral yield hydroxy, methoxy and ethoxy derivatives with alcoholic potash, sodium methylate and sodium ethylate In each case one chlorine atom is replaced.
2. The *m*-nitraniline-chloral product is so sensitive to these basic reagents that each of them in the cold breaks it up into its constituents.
3. The nitro group in the benzene ring of the amine stabilizes the Schiff's base to such an extent that basic reagents yield derivatives, though this is not true when it is in the *meta* position.

CHAPEL HILL, N. C.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF COLUMBIA UNIVERSITY, No. 326.]

INFLUENCE OF ASPARTIC ACID AND ASPARAGIN UPON THE ENZYMIC HYDROLYSIS OF STARCH.

BY H. C. SHERMAN AND FLORENCE WALKER.

Received August 29, 1919.

In 1893 Effront[1] stated that asparagin accelerates the hydrolysis of starch by malt and taka-diastase. A few years later[2] he obtained similar activation by addition of certain proteins and of a boiled cold water extract of barley. In 1904 he reported[3] that asparagin, aspartic acid, hippuric acid, creatin, creatinin, and the peptones increased the action of malt extract, while succinamide, the amines and their salts, and acid amides generally act unfavorably. This he found for several starches of different origin. He also found, however, that the more favorable the conditions for production of an optimum amount of sugar, the less marked is the effect of the amino acids.

Ford,[4] working with malt, found asparagin to be without effect on the activity of the enzyme. The apparent activation by amino acids and acid salts obtained by other investigators, he ascribes to the neutralization by these compounds of alkaline impurities in the starch.

According to Terroine and Weill[5] saccharification by pancreatic juice is greatly accelerated by α-alanine, glycine, leucine, valine, histidine, arginine, tyrosine, phenyl-alanine, aspartic acid, and glutamic acid. The activating power which they found the digestion products of protein to possess is, they think, most probably due to the amino-acids formed.

More recently Rockwood[6] has investigated the effects of several nitrogenous substances on the hydrolysis of corn starch by saliva and concludes that glycine, tyrosine, anthranilic acid and its *meta* and *para* isomers, aspartic acid, hippuric acid, proteins (serum albumin and gelatin) and amines of the methane series increase saccharification, whereas the amides (acetamide, propionamide and urea) sulfanilic acid, asparagin, succinimide and succinamide show no such effect. He also found that glycine and aspartic acid activate pancreatic extract.

Because of the lack of agreement among previous workers as to whether amino acids do or do not activate amylases, and in view of the fact that past investigations have seldom covered more than one enzyme, a systematic study of the influence of amino acids upon the action of several amylases, in purified as well as in their natural or commercial forms, seemed desirable.

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[1] *Mon. sci.*, 41, 266 (1893).

[2] *Compt. rend.*, 120, 1281 (1895).

[3] *Bull. soc. chim.*, [3] 31, 1230 (1904); *Mon. sci.*, [4] 18, 561 (1904); *Compt. rend. Soc. Biol.*, 57, 234 (1904)

[4] *J. soc. Chem. Ind.*, 23, 414 (1904).

[5] *Compt. rend Soc. Biol.*, 72, 542 (1912).

[6] THIS JOURNAL, 39, 2745 (1917).

Experimental.

Apparatus and Materials Used.—Description of apparatus, its selection and care, has been given in previous papers from this laboratory.

The starches used were potato, wheat, maize and rice starches purified in the laboratory by washing with cold, very dilute sodium hydroxide and water as described in a previous paper, and Merck's "soluble starch according to Lintner," washed 9 times with ordinary distilled and 6 times with triply distilled water. 100 cc. of a 1% dispersion, made neutral to rosolic acid with 0.01 *N* alkali or acid, were used for each digestion.

The enzyme preparations employed were those described in our recent paper upon rate of hydrolysis of starches of different origin.[1]

The water extract of potato was obtained by letting one grated potato of medium size stand overnight in 150 cc. of purified distilled water. This was filtered and the filtrate boiled. Its acidity was carefully determined, rosolic acid being used as indicator. Well purified specimens of aspartic acid and asparagin were used. The exact amount needed for each experiment was weighed out and dissolved in the least possible volume of triply distilled water plus the amount of alkali necessary for neutralization.

Method.—The procedure has been fully described in previous papers. When water-washed or alkali-washed starch was used as substrate, the amount of reducing sugar was determined by Fehling's volumetric method.[1] With Lintner's "soluble" starch the gravimetric method[2] which has been used in this laboratory since 1910 was usually employed. The potato extract and the aspartic acid and asparagin solutions were added to the starch dispersions in the cylinders after cooling and before adjusting to final volume.

Experiments with Potato Extract.

In recent experiments[1] on the action of enzymes upon starches of different origin, we found that, when similarly purified by washing with cold, very dilute alkali or with such alkali and then with ether (in either case followed by very thorough washing with pure water) all the starches tested were of practically equal digestibility. This was true whether the digestive agent employed were saliva, pancreatin, malt extract, taka-diastase, or a laboratory preparation of purified amylase of pancreas, malt or *Aspergillus orysae*, except that in experiments in which purified pancreatic amylase acted upon purified potato starch the results obtained were abnormally low. In this particular case it appeared that the rigorous "purification" of both starch and enzyme had in some way diminished the facility of interaction between them. Addition of a small amount of boiled, carefully neutralized, water extract of potato to the digestion mixture resulted in hydrolysis at a fully normal rate.

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[1] Sherman, Walker and Caldwell, THIS JOURNAL, 41, 1123 (1919).

[2] Sherman, Kendall and Clark, *Ibid.*, 32, 1082 (1910)

When such potato extract was added to the purified starch substrates which had shown normal digestibility, the rate of hydrolysis appeared to be increased slightly, not only in the case of purified pancreatic amylase, but also of commercial pancreatin and saliva. Upon the action of purified amylases of malt and *Aspergillus oryzae*, however, potato extract had much less, if any, effect. In all cases it appeared that, in the presence of a small amount of the water-soluble substances of the potato, potato starch was digested quite as readily as that of either wheat, maize or rice.

TABLE I

Effect of 1 cc. Potato Extract upon Enzymic Hydrolysis of Starch.

	Per cent of starch hydrolyzed in 30 min. by					
	Purified pancreatic amylase (No 62)		Pancreatin		Saliva	
Description of starch.	Without potato extract	With potato extract	Without potato extract	With potato extract	Without potato extract	With potato extract
Wheat starch (alkali washed)		42.2	36.0	38.8	40.2	44.3
Maize starch (alkali washed) ..	37.5	42.0			40.6	45.8
Rice starch (alkali washed) .	37.0	40.5			41.5	46.3
Potato starch (alkali washed) .	25.5	47.7			43.5	49.6
Potato starch (water washed) .	38.4	47.3	37.3	40.3		
Potato starch (Lintner "soluble")	39.2	45.0				

TABLE II

Effect of 1 cc. Potato Extract upon Enzymic Hydrolysis of Starch.

	Per cent. of starch hydrolyzed in 30 min by			
	Purified malt amylase (No 155)		Aspergillus amylase (prep 22)	
Description of starch	Without potato extract.	With potato extract.	Without potato extract.	With potato extract
Wheat starch (alkali washed)	38.4	39.1	38.6	40.1
Potato starch (water washed)	41.0	40.8	39.9	41.1

Since the activating material in the potato extract was water-soluble and heat-stable and the optimum amounts of chloride and phosphate were added to the starch substrate in all cases whether potato extract was to be added or not, attention is naturally directed to the amino acids and acid amides as possibly responsible for the effect of the potato extract.

Experiments with Aspartic Acid and Asparagin.

The results of experiments on the influence of aspartic acid, carefully neutralized with sodium hydroxide, upon the rate of hydrolysis of different starches by different enzymes are shown in Tables III-V. The methods employed were those described in our previous paper mentioned above, and, as in that case, only the data of experiments in the same table and by the same digestive agent are directly comparable with each other.

TABLE III

Effect of Various Amounts of Aspartic Acid (Neutralized by Sodium Hydroxide) upon the Hydrolysis of Starch by Purified Pancreatic Amylase

Description of starch	Aspartic acid added (weight before neutralization) Mg	Starch digested in 30 min %
Water washed potato starch	None	38.8
	50	45.2
	100	44.2
Lintner soluble starch	None	39.1
	30	41.5
	50	44.9
	100	43.3

TABLE IV

Effect of Neutralized Aspartic Acid upon the Hydrolysis of Starches by Saliva, Pancreatin and Purified Pancreatic Amylase

	Per cent of starch hydrolyzed in 30 min by					
	Saliva		Pancreatin		Pancreatic amylase prep 62	
Description of starch	Without aspartate	With aspartate	Without aspartate	With aspartate	Without aspartate	With aspartate
Alkali washed						
Wheat starch	41.1	47.4	40.1	44.6	36.5	40.3
Maize starch	40.7	48.0	40.5	44.8	36.7	43.2
Rice starch	41.6	49.8	41.1	43.8	37.4	40.3
Potato starch			41.2	47.9	25.7	43.6

TABLE V

Effect of Neutralized Aspartic Acid upon the Hydrolysis of Starches by Malt Extract, Taka-Diastase and the Amylase Preparations Obtained from them

	Per cent of starch hydrolyzed in 30 min by							
	Malt extract		Malt amylase (prep 155)		Taka diastase		*Aspergillus* amylase (prep 22)	
Description of starch	Without aspartate	With aspartate	Without aspartate	With aspartate	Without aspartate	With aspartate	Without aspartate	With aspartate
Alkali washed								
Wheat starch	54.7	54.5	40.2	45.3	50.0	51.0	42.4	42.8
Maize starch	53.8	53.3	41.8	47.5	51.0	51.7	40.7	40.5
Rice starch	54.7	55.1	42.0	44.6	53.0	53.8	41.1	40.9

Tables VI and VII show the influence of aspartic acid and asparagin upon the hydrolysis of Lintner soluble starch by the various amylases. The amount of reducing sugar formed was determined gravimetrically and, for convenience of comparison with the results of previous workers, is indicated in the tables by the number of mg. of cuprous oxide found after correction by blank experiments with the starch and reagents.

TABLE VI.

Effect of Neutralized Aspartic Acid and Asparagin upon Hydrolysis of Lintner Soluble Starch by Saliva, Pancreatin and Purified Pancreatic Amylase.

Aspartic acid, Mg	Asparagin, Mg	Mg cuprous oxide. Saliva.	Pancreatin.	Pancreatic amylase No. 59.
None	None	342	322	277
50	None	371	340	306
100	None	381	336	305
None	50	380	341	306
None	100	391	343	312
50	50	384	342	305
25	25	379	341	310

TABLE VII

Effect of Neutralized Aspartic Acid and Asparagin upon Hydrolysis of Lintner Soluble Starch by Malt Extract, Taka-Diastase and the Amylase Preparations Obtained from Them.

Aspartic acid, Mg	Asparagin, Mg.	Malt extract.	Mg cuprous oxide Malt amylase No 155.	Taka-diastase.	*Aspergillus* amylase 22.
None	None	191	209	291	258
50	None	196	212	291	260
100	None	.	220	294	261
None	50	195	223	295	260
None	100		218	299	265
50	50	196	220	295	264
25	25	196	222	295	263

It will be seen from Tables I to VII that the addition of a small amount of neutralized aspartic acid not only corrects the tendency to abnormally low results in the case above noted, but also appreciably increases the rate of action of saliva, pancreatin, purified pancreatic amylase and purified malt amylase upon all of the starches here tested. Under the conditions of our experiments it had no appreciable effect upon the action of malt extract, taka-diastase or the laboratory preparation of *Aspergillus* amylase.

Asparagin behaves in like manner except for what appears to be a very slight activation of taka-diastase and purified *Aspergillus* amylase, which may be due to some unrecognized experimental error.

The above tables also show that the addition of both aspartic acid and asparagin to the same digestion mixture does not result in greater activation than one of the compounds alone would produce, when used in optimum concentration.

A comparison of the results obtained with potato extract on the one hand, and with aspartic acid or asparagin on the other, brings out the fact that the former did not activate malt amylase, while the pure substances appeared to do so. A possible explanation of this is that the direct cause of the increased amylolytic activity is in all such cases amino acids rather than protein. Potato extract in the small quantity used might furnish too little preformed amino acid to produce a distinct activation. The pancreatic enzymes and saliva being proteolytic as well as amylolytic could form activating amino acid from the protein of the potato extract, while purified malt amylase, being protease free, derived no such benefit.

As noted above, activating effects of amino acids upon the digestion of starch have been reported by some previous experimenters while others have held that such observations do not indicate a true activation, but only a favorable influence of the added amino acid upon the hydrogen ion concentration of the digestion mixture. In order to test this point the hydrogen ion concentrations of our digestion mixtures with and without the added (neutralized) aspartic acid and asparagin were determined electrometrically. Typical results are shown in Tables VIII and IX.

TABLE VIII.

Rate of Digestion and Hydrogen Ion Concentration with and without Neutralized Aspartic Acid.

	Pancreatic amylase prep 62	
	Without aspartate	With aspartate
Expt 1		
Starch hydrolyzed in 30 min., %	35.8	42.3
Hydrogen ion concentration as P_H	6.63	6.68
Expt 2		
Starch hydrolyzed in 30 min., %	40.5	47.7
Hydrogen ion concentration as P_H	6.63	6.62

TABLE IX

Effect of Neutralized Asparagin on Hydrogen Ion Concentration.

Solutions activated as for digestion by malt amylase.

Asparagin (before neutralization) Mg.	None	50	100	100
Hydrogen ion concentration as P_H.	4.95	4.94	4.95	4.96[a]

Solutions activated as for digestion by taka-diastase.

Asparagin (before neutralization) Mg	None	50	100	100
Hydrogen ion concentration as P_H	5.31	5.31	5.39	5.33[a]

[a] Determined before digestion. Other determinations made at end of digestion.

In Expt. 1, Table VIII, neutralization of aspartic acid was governed simply by titration of solution with rosolic acid as indicator. In Expt. 2, guided by electrometric measurements made in Expt. 1, a little less alkali was used to "neutralize" the added aspartic acid. These results (Tables VIII and IX) show plainly that, in our experiments at least, the activating effect of sodium aspartate or of asparagin is not attributable to change in the hydrogen ion concentration of the digestion mixture.

The accelerated transformation of the starch to reducing sugar in the presence of the sodium aspartate or of asparagin is, therefore, not referable to hydrogen ion concentration. Neither is it referable to the sodium ion nor to the mere concentration of electrolyte since, in all of the experiments with pancreatic amylase, optimum concentrations of sodium chloride and sodium phosphate were present.

While sodium aspartate results in higher activity of pancreatic amylase than can be induced by sodium chloride and sodium phosphate alone, it was also found by further experiments that the aspartate cannot replace the chloride in the activation of this enzyme. The percentages of starch digested in 30 minutes by purified pancreatic amylase in the presence of different combinations of these 3 salts were as follows:

With phosphate and chloride	41 2%
With phosphate, chloride and aspartate	48 3%
With phosphate and aspartate only	25 8%

In this connection we may recall the fact shown in previous papers that our purified pancreatic amylase (the most active enzyme of which we have knowledge when tested in the presence of proper concentrations of chloride and phosphate) shows no activity in the absence of added electrolytes.

The experiments described in the present paper show, therefore, a rather specific effect of the amino acids tested in that they induced still further activity in the enzyme already "fully activated" by the addition of optimum amounts of chloride and phosphate

Summary.

The action of saliva, pancreatin, and purified pancreatic amylase on alkali-washed potato, wheat, maize and rice starches and on Lintner "soluble" starch was accelerated by the addition of small amounts of boiled, neutralized water extract of potato, while the action of the vegetable amylases tested was not influenced by the addition of the potato extract.

The addition of neutralized aspartic acid or asparagin accelerated the action of saliva, pancreatin, and purified pancreatic and malt amylases. Clear evidence of activation was not obtained in the case of malt extract, or the preparations made from *Aspergillus oryzae.*

The addition of both sodium aspartate and asparagin to the same digestion mixture produces practically the same activation as does one of these substances alone. Thus the activating effects of these substances are interchangeable rather than additive.

In what sense is this activation specific? It was not due, in these experiments, to change in hydrogen ion concentration, nor merely to a more favorable concentration of electrolyte. The amino compounds to be tested were added to a substrate which already contained the optimum concentrations of sodium chloride and phosphate, the reported activation being thus additional to the activity induced by chloride and phosphate. Moreover, sodium aspartate is not interchangeable with sodium chloride in the activation of purified pancreatic amylase.

The work is being extended to a similar study of the effects of other amino acids.

We are greatly indebted to the Carnegie Institution of Washington for grants in aid of this investigation.

NEW YORK N Y

[CONTRIBUTION FROM THE LABORATORIES OF PHARMACEUTICAL CHEMISTRY, UNIVERSITY OF WISCONSIN]

REDUCTION OF DIHYDROXY-THYMOQUINONE BY MEANS OF PALLADIUM-HYDROGEN.

BY NELLIE A WAKEMAN

Received September 5, 1919

Thymoquinone and its oxidation and reduction products form an interesting series of compounds which have, from time to time, received considerable attention at the hands of organic chemists. The writer's interest in these compounds was aroused by the seemingly important role which they appear to play in the pigmentation of several species of *Monarda*, and it has been held no less by the behavior of the substances themselves than by their biochemical significance.

Two or three years ago, in reviewing the work of Pall[1] and Skita[2] upon the hydrogenation of organic compounds by means of palladium as a catalyst, it was learned that one of them[3] had in this manner reduced quinone to hydroquinone. The question of the action of thymoquinone toward this reagent therefore naturally presented itself, and accordingly the action was tried in alcoholic solution. Thymoquinone reduced very readily. Upon evaporation of the solvent, it yielded hydrothymoquinone which was identified by its melting point, its solubility, and its crystalline form.

The reduction of thymoquinone to hydrothymoquinone ordinarily presents little difficulty. A more interesting reaction promised to be the reduction of dihydroxy-thymoquinone to tetrahydroxy-cymene by the same reagent.

Zincke,[4] in 1881, reduced the mother liquors from which dimethylamino-thymoquinone had crystallized, by the use of sulfurous acid, thus obtaining a solution which, upon oxidation, yielded a mixture of mono- and dihydroxy-thymoquinone. Zincke believed that the reduced liquid contained a solution of both tri- and tetrahydroxy-cymene. All attempts of the writer to produce these polyatomic phenols by the reduction of the corresponding quinones had hitherto proved fruitless.

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[1] *Ber.*, 38, 1401, 2414 (1905); 40, 1392, 2201 (1907); 41, 805, 818, 2272, 2287 (1908), 42, 1572, 2239, 3930 (1909)

[2] *Ibid.*, 41, 2938 (1908), 42, 1627 (1909); 43, 3393 (1910); 44, 2862 (1911); 45, 1948 (1912).

[3] *Ibid.*, 43, 3393 (1910)

[4] *Ibid.*, 14, 92 (1881).

Following the reduction of thymoquinone, a small quantity of dihydroxy-thymoquinone was treated in the same way. The reduction took place very readily, marked by the change in color of the solution from red, or yellow, to water white. Before the solvent could be evaporated, however, the color returned and crystals of the original red compound separated out. Ether was next chosen as a solvent. The reduction took place even more readily than before. The same difficulty, to a less degree, was experienced in obtaining the products of reduction in a solid form, for though flaky, white crystals of the reduced compound were obtained upon evaporation of the solvent, red needle-like crystals of the original substance formed almost simultaneously, the mass took on a pinkish gray color, and finally changed to red dihydroxy-thymoquinone with its characteristic melting point of 226°. By evaporating the ether in an atmosphere of hydrogen an abundance of pure white, flaky crystals was obtained. Upon removal from the reducing atmosphere, however, these became mixed with the red needle-like crystals before even a melting point could be determined. This mixture, upon standing, passed through the process of changing, through pinkish gray, back to red.

The red dihydroxy-thymoquinone was next dissolved in acetic acid anhydride and subjected to the same reducing process, the object being to transform some, or all, of the hydroxy groups to acetyl groups, thus rendering them more stable. This reduction took place more slowly; nevertheless, it was completed in the course of a few hours. Upon the evaporation of the greater portion of the solvent, the reduced product crystallized out in white, prismatic crystals which melted at 180–182° and exhibited a saponification value[1] equal to that required for 4 acetyl groups. The tetraacetyl derivative thus obtained is stable in the air. The yield[2] is almost quantitative. Upon hydrolysis of the acetyl derivative, practically all of the dihydroxy-thymoquinone started with can be recovered.

In carrying out the above reduction another change, which will be further investigated, was noted. Part of the acetic acid anhydride appears to have been reduced and an ester of some sort to have been formed. At any rate, when a portion of the freshly reduced solution was strongly diluted with cold water a pleasant fruity odor, resembling somewhat both ethyl and amyl acetates, but differing from either, was developed. Upon standing a short time in contact with water this pleasant odor disappeared. Moreover, it could not be obtained from the reduced solution which had stood for some time in the air.

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[1] Subs., 0.504.

Used 24 cc. KOH solution, factor 0.3936 = 94.46 cc. 0.1 *N* KOH.

To neutralize required 55.3 cc. 0.1 *N* HCl.

To saponify required 39.16 cc. 0.1 *N* KOH.

Calc. for 4 acetyl groups 38.9 cc. 0.1 *N* KOH.

[2] From 0.5 g. of dihydroxy-thymoquinone a little more than 0.8 g. of the tetraacetyl derivative was obtained.

All of the above reductions were carried out in a simple reduction flask, prepared by turning up the ends of an ordinary 250 cc. gas sampling tube with two glass stopcocks. The hydrogen was generated from zinc and hydrochloric acid and passed through first an alkaline and then an acid solution of potassium permanganate. After this it was passed through sulfuric acid and then into the reduction flask. During the first reductions a shaking machine was used for shaking the flask; but the process went on so readily that this was not necessary. At first, also, the palladium chloride used was placed in a little water with a very small quantity of mucilage of acacia added to hold the resulting palladium in suspension. This also, was found unnecessary, even undesirable. In all of the later work a concentrated, warm, solution of the substance to be reduced was placed in the reduction flask. It usually crystallized out upon cooling. About 0.1 g. of palladium chloride was suspended in a little of the same solvent and added to the solution in the flask. Hydrogen was now passed through the flask until most of the air had been replaced, when the exit tube was closed. After this the flask was shaken occasionally until the reduction was complete. In using ether as a solvent, it was found necessary to fill the flask with hydrogen and close both stopcocks, opening the inlet only to pass in more hydrogen, from time to time, as it had been absorbed, otherwise the pressure of the ether was often greater than that of the hydrogen and trouble resulted.

For the greater part of the above work the same charge of palladium chloride, 0.1 g. was used over and over again without any sign of exhaustion of its catalytic property. The reduced solution was poured out through a filter. The palladium remaining in the flask, and that on the filter, was washed with a small portion of the pure solvent, then, repeatedly, with alcohol and ether. The portion of palladium upon the filter was carefully returned to the flask and another reduction was carried out. In this way a large number of reductions were made without the addition of fresh palladium chloride, several different substances, each in two or three different solvents, being reduced. Whether or not the change of substances, and of solvents, had any influence upon the presistent power of the catalyst is not known. It certainly retained this power to a remarkable degree, the only evidence of the catalyst "wearing out" noticed being the small loss incurred by adhesion to the filter.

MADISON, WIS.

NOTE.

Correction.—The formula for methylguanido-glyoxylic acid, given on page 1110 of the July, 1919 number should read $NH_2C(NH)NCH_3$.-COCOOH.

Isidor Greenwald.

NEW BOOKS.

The Preparation of Substances Important in Agriculture. A Laboratory Manual of Synthetic Agricultural Chemistry. 3rd Edition. By Charles A Peters, Ph.D., Prof. of Inorganic and Soil Chemistry, Dept of General and Agricultural Chemistry, Mass. Agricultural College. John Wiley and Sons, Inc , New York: Chapman and Hall, Ltd , London, 1919. vii + 81 pp. 13 × 19 cm. $0 80.

The laboratory course outlined in this small volume makes use of the preparation of substances important in agriculture to train the student who has already had a one year course in chemistry at high school, or its equivalent. The table of contents includes: Superphosphate, Sulfate of Ammonia, Potassium Nitrate, Potash Salts, Lead Nitrate, Lead Arsenate, Lime-Sulfur, Copper Sulfate, Paris Green, Bordeaux Mixture, Emulsions.

Under each of these headings the main object of the process is first stated; the laboratory directions are then given; following this are notes on the chemical, commercial, and agricultural aspects of the subject; lastly comes a series of questions to be answered by the student in the laboratory note book.

Many teachers are of the opinion that the kind of laboratory work presented in this book is of the greatest value as chemical training. The experiments are sustained, so that the interest centers on one point over a considerable period of time. Incidental problems come up in connection with the major problem, so that they have a significance they would not possess if they were taken as independent experiments. There is a distinct incentive to use judgment and skill in manipulation because the amount and quality of the final product are influenced thereby. Professor Peters remarks in his Preface: "The method of presentation aims to put a few major points before the student and extend the work on such points over so long a time that the student will absorb it. The author feels that when a student, in his earlier years in college, works interestedly for a whole exercise around one thing he grasps something while if a dozen important points pass in review during the time he is left in a maze and gets little but technical benefit. While, however, the student is busy on the one major piece of work other minor points may be gathered round it and readily absorbed."

A trip over the northern peaks of the White Mountains from which the reviewer has just returned, although somewhat remote from chemistry, offers a convenient analogy. He found those peaks swarming with young girls from the various girls' camps. This was delightful on one of the days which was sunny, but horrible on one of the days which was rainy, when 74 girls arrived at the Madison Hut (which has bunks for 46) All were wet and cold and hungry; they had no change of clothing and they had to sleep in wet things, some of them on the floor. They were being guided by inexperienced young women councillors who did not know the mountains well. The prospectuses all advertise the hike over the northern peaks as one of the features of the camp life, and the camp directors therefore feel it is imperative to send the children off on the hike even if it is inadequately prepared for.

Many topics in first year text books and manuals of chemistry are rushed into with inadequate preparation because the author has not the courage to leave them out. There is probably no writer of such books that has not been guilty of this sort of offense. The subject of colloids is certainly of great importance in agricultural chemistry. Professor Peters briefly discusses colloids in the chapters on lead arsenate, and emulsions. The subject is as fascinating as the high peaks in sunny weather, but if the student expects to understand the principles which are very briefly stated in the text, he is likely to find himself like the hiker in a dense and chilly fog on the high ridge, with precipices in most directions and the trail lost. This is not said in condemnation but simply in emphasis of the fact that judgment in choice of topics and their presentation is the most important factor in planning a course for students who are not far advanced. It is probably true that mention of colloids could not have been omitted from such a manual of agricultural substances.

In conclusion, the book under review must prove of great value to students of agricultural chemistry, for it is essentially a laboratory course in the fundamental principles of chemistry, using substances important in agriculture as illustrations. Excellent judgment has been shown in the selection of material for the experiments and topics for the discussions and questions. ARTHUR A. BLANCHARD.

Introduction à la Chimie Générale, Lois Fondamentales de l'Atomisme et de l'Affinité Exposées à des Chimistes Débutants By H COPAUX Gauthier-Villars et Cie., Paris, 1919 208 pp 18 × 11.5 cm

In the preface, the author states it as his intention to reduce the number of false starts made by students who depend upon oral instruction and lecture notes. The reviewer, however, suspects that many college students, even after 4 years' study of chemistry, have not mastered the ground covered by the book. Two hundred small pages contain a remarkably complete outline of the subjects foreshadowed by the title, including 53 pages dealing with the properties and theories of solutions. The advanced student will be astonished to find experimental methods, data, diagrams, and discussions for so many generalizations, all compressed into so small a space without appearance of haste or lack of clarity. Sympathy is felt, nevertheless, for "debutants," confronted on page 5 by $\Delta m = \Delta E/V^2$, and so on. One can only hope that they, like most "debutantes," have already been vouchsafed at least an informal view of the intricacies among which they must function. Lack of balance is sometimes, though not often, sensed, 5 pages, for instance, on supersaturation of salts in water solution and 12 on the ionization theory, including conductivity and hydrolysis. The difficult field of concentrated solutions, so profitably explored of late years by Washburn and others, is avoided except for a discussion of solubility. But how much easier to criticize than to plan a book half as meritorious! One closes it with profound respect for the vitality and elegance of French instruction in chemistry. G. S. FORBES.

Chimica delle sostanze esplosive. By MICHELE GIUA, Professor of General Chemistry in the University of Sassari 556 pages, 83 figures and 7 tables Ulrico Hoepli, Milan, 1919 L. 28.

The author treats his subject in 6 parts, the first dealing with the historical development of the knowledge of explosives during the nineteenth century, the principles of thermochemistry, the gas laws, Nernst's theory, explosion temperatures, pressures and, potential and other generalities; the second with definite explosive compounds; third, explosive mixtures; fourth, explosive gases and detonating gaseous mixtures; fifth, primarily unstable substances; and sixth, chemical and physical tests of explosives; a classification which works out admirably in bringing related substances together and permitting of a systematic treatment of a group. The book is supplied with an admirable table of contents and excellent indexes of authors and subjects. Of the remaining 524 pages devoted to subject matter part one occupies 16% of the space, two 49, three 16, four 1, five 6 and part six 12%. But as the fulminates, hydronitrides and diazo compounds treated of in part five are as truly explosive compounds as any in part two, there is really 51% of the space devoted to the primary explosive bodies. Of the 252 pages in part two 161, or 64%, are devoted to the nitro derivatives of aromatic hydrocarbons and 91, or 36%, to the nitro and nitric derivatives of the aliphatic hydrocarbons. Or noting with more particularity it is observed that 6% of this space is assigned to naphthalene and its derivatives, 10 to benzene, 12 to glycerin, 13 to phenol, 15 to cellulose, and 25% to toluene and its derivatives. Considering the fact that, excepting the members of the gunpowder class, in general all explosive mixtures derive their significant characteristics from explosive compounds with which modifying components are admixed, and considering the further fact that the nitro substitution derivatives of the aromatic hydrocarbons, and especially those from toluene, have in recent years played a most important part as explosives, good judgment has been exercised in the allotment of space to the various substances and subjects treated.

The method of treatment is excellent, being concise, simple and direct while space is conserved and use of the information collected facilitated by the presentation of the data in numerous well designed tables and the liberal use of graphs and diagrams. The writer has adhered more closely to his text than writers on the chemistry of explosives usually do and has completely resisted the temptation to describe the applications and uses of explosives. He has dwelt on the technology but only as regards the manufacture of explosives which, for explosive compounds, are strictly chemical operations. Even in these instances he has restricted his description of the parent substances in each case to that one which is the source of the positive radicals in the product. As nitric, sulfuric, and mixed acids, sodium nitrate, alcohol, acetone, and the other reagents generally used in these operations are already dealt with in great detail and in an authoritative manner by Lunge and others, it is evidently unnecessary to repeat such descriptions. However Giua does include tables of specific gravities of several of them in the section of his book devoted to tests, and essential data for them, such as the most suitable strengths and best proportions for nitration mixtures and the like, are given elsewhere when important or recently determined. The technological descriptions are brief, covering, as a rule, only the essential principles. One who intended erecting a manufacturing plant would find more complete details of construction and operation elsewhere, but he would find here much suggestive data which is not usually given in strictly technological books.

The author has, in this development of his text, placed the emphasis on the pure chemistry rather than the applied chemistry phase, and more particularly on that of physical chemistry. Thus in approaching the subject of nitro-aromatics he devotes a section to the reactivity of the nitro-groups in aromatic compounds, stating and discussing here the laws of Laubenheimer and of Koerner, while, as those acquainted with the author's own researches might expect, eutectic temperatures and equilibrium curves are given for many different systems.

The footnote references which abound on nearly every page show a wide acquaintance with the best authors and they constitute a most valuable bibliography of explosives. The publications of investigators in the United States are more generally cited than is usual with European authors and the citations are quite up to date, E. J. Hoffman's recent report on his excellent investigation of the nitration of toluene, for instance, being presented in considerable detail.

The fulness of treatment of topics may be illustrated by the nitrogen containing derivatives of glycerin under which appear detailed accounts of the mono-, di- and trinitroglycerin, tetranitro-isobutyl-, tetranitrodi- and chloro-dinitro-glycerin, in the course of which due consideration is given to Hibbert's study of the tautomerism of trinitroglycerin, and Snelling and Storm's determination of the detonation temperature. Among the explosive mixtures in part three one is surprised to find so large a proportion of the space devoted to chlorate and perchlorate powders. It is possible that Giua is one of the not inconsiderable number of the students of explosives who believe that the chlorate or perchlorate mixtures may yet be so controlled as to play a useful part, a hope based on the knowledge that they are cheap sources of energy. Most of the special compositions and some of the compound substances which played a significant part in the Great War are not mentioned but it is surprising that the U. S. composition should be omitted from the section on smokeless powders, which section is perhaps, considering the amount of literature available on the subject, the least satisfactory part of a very satisfactory book. Considering that hexanitrodiphenyl sulfide was an enemy product and weapon its omission is also surprising.

The book is made up in a most attractive form with good paper, wide margins, clear impressions and intercalated titles. Errors appear to be but few and most of those have been already noticed in the appended "Errata-Corrige." In addition to these we notice that on page 184 Koerner is spelled "Korener." It is suggested also that on page 38 the heat of explosion of one kg. of nitroglycerin should be stated as 1570.5 cal. instead of 1781 cal. as at present. These are of inconsequence in view of the marked excellence of the work and the spirit of approach of the author voiced in his opening paragraph on the Historical Development during the Nineteenth Century in the following phrase *La scienza degli esplosivi fu fondata da Berthelot di immortale memoria.*

CHARLES E. MUNROE.

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REPORT OF THE INTERNATIONAL COMMITTEE ON ATOMIC WEIGHTS FOR 1919-20.

Received September 29, 1919

The last regular report of this committee, apart from an annual recommendation to continue the use of the table of atomic weights then presented, was published in 1916. The interruption in the series of reports was, of course, due to the world war, which created difficulties of a serious kind among all international organizations. Coöperation with Germany became impossible, partly because of the difficulty of correspondence, and partly because of the personal hostilities created by the conduct of the war. There was also an inevitable slackening of scientific activities, and this was well shown by the unusually small number of new researches in the field of atomic weights. Now that peace is in sight, it seems wise to resume the preparation of these reports, even though they may not be for some time quite so truly international as heretofore. The determinations published since the preparation of our last report may now be summarized as follows:

Hydrogen.—A very thorough investigation by Burt and Edgar[1] on the volumetric composition of water has given the volume ratio of hydrogen to oxygen as 2.00288 : 1. From this value, taking the normal liter weights of oxygen and hydrogen as 1.42900 and 0.089873 g., respectively, the atomic weight of hydrogen becomes 1.00772, or, rounded off, 1.0077. Guye,[1] from a discussion of Burt and Edgar's data, accepts this value as lying between the two extremes of 1.00767 and 1.00773. If, however, instead of trusting to the densities of the gases and their physical constants exclusively, we take into account the admirable researches of Morley, Noyes, and others, upon the synthesis and analysis of water,[2] the most probable general mean for the atomic weight of hydrogen becomes 1.0078, which differs from the volumetric value by only 1/10000. That is, the two distinct lines of attack upon the problem agree within the limits of actual uncertainty. For ordinary purposes the approximate value 1.008 is close enough. It must be remembered that the tables prepared by this committee are for the use, not so much for specialists, as for working chemists in general; and too much refinement will only lead to confusion. No determinations of these or any other constants can be absolute and final. All are subject to errors which may be reduced nearly, but not quite, to insignificance, but never eliminated entirely. For example, in the determination of atomic weights from gaseous densities it is not possible to guarantee the *absolute* purity of the gases, or to avoid errors in weighing, in reductions to a vacuum, or in the values given to the physical constants that are used in the final computations. Some of these errors may be so small as to be negligible, and in the aggregate they may tend either to reinforce or to compensate one another, but their extreme magnitude can be estimated with some approach to accuracy, and expressed by means of the usual ± sign. At present an accuracy to within 1/10000 is the best we can expect to obtain.[3]

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[1] *Phil. Trans.*, 216A, 393 (1916). This research was noted in the previous report for 1917. Its review by Guye renders its repetition desirable here.

Carbon.—Two investigations on the atomic weight of carbon were reported from the Geneva laboratory in 1918. First, Stahrfoss[4] determined the density of acetylene, ethane, and ethylene. Acetylene proved to be unsatisfactory, because of its tendency to polymerize. From ethane he obtained the value C = 12.006, and from ethylene C = 12.004. On account of some uncertainties in the reduction, he prefers, provisionally, the value C = 12.00.

Secondly, Batuecas[5] determined the density of ethane, and reduced his observations by 3 methods, giving C = 12.005, 11.999, and 11.996. The last two being concordant he regards as preferable, and their mean, C = 11.998, he adopts. It will be remembered that Richards and Hoover, by purely chemical methods, found C = 12.005; and a later combination of all determinations published before 1918 gave the chairman of the committee the mean value C = 12.0025. For ordinary purposes the rounded-off value C = 12.00 may be used, and is so given in the table.

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[1] *J. chim. phys.*, 15, 208 (1917).

[2] Computation by F. W. C.

[3] For an elaborate discussion of sources of error in atomic weight determinations, see Guye and his colleagues (M. Germann, Moles and Renard) in *J. chim. phys.*, 14, 25, 195, 204 (1916); 15, 60, 360, 405 (1917); 16, 46 (1918).

[4] *Ibid.*, 16, 175 (1918).

[5] *Ibid.*, 16, 322 (1918).

Bromine.—Three sets of determinations of the molecular weight of hydrogen bromide have been made in Guye's laboratory at Geneva, by Moles,[1] Reiman,[2] and Murray.[3] The acid used was prepared by several distinct methods, and all gave concordant results, which may be summarized as follows, when H = 1.0078:

	Mol wt HBr	At wt Br
Moles .	80.9332	79.9254
Reiman	80.932	79.9242
Murray . .	80.930	79.9222

These values are wonderfully concordant and the variations are far within the allowable limits of experimental error. In a recent combination, by the chairman of this committee, of all the available data relative to the atomic weight of bromine, the value found was Br = 79.9228, in complete harmony with the Geneva determinations. For ordinary purposes the rounded-off figure 79.92 is enough.

Boron and Fluorine.—In a very original investigation Smith and Van Haagen[4] have simultaneously redetermined the atomic weights of boron and fluorine. Their starting point was anhydrous borax, $Na_2B_4O_7$, and their chief difficulty was in insuring the complete dehydration of that compound. The salt was then converted, in a series of successive experiments, into sodium sulfate, carbonate, nitrate, chloride and fluoride, which gave 8 independent values for boron ranging from 10.896 to 10.905, in mean, 10.900. This value was computed with Na = 22.997, Cl = 35.457, S = 32.064, N = 14.010, and C = 12.005. The authors finally discuss all previous determinations and show wherein they were affected by errors. The new value 10.900 should be adopted as the most probable.

In this research sodium fluoride was compared not only with borax but also with the sulfate, and the 8 values found ranged from 19.002 to 19.008, in mean 19.005. The rounded-off value F = 19.0 may be retained for all practical purposes.

Lead.—Oechsner de Coninck and Gérard[5] have attempted to determine the atomic weight of lead by calcination of the nitrate; and find Pb = 206.98 when N_2O_4 = 108. This determination is evidently of no present value. With this exception the other recent researches relative to this constant have referred to isotopic lead, and the normal element is considered only in comparison with it. Richards and Wadsworth,[1] for instance, find for normal lead $Pb = 107.183$, and Richards and Hall[2] give $Pb = 207.187$, values slightly lower than the accepted 207.20 as determined by Baxter and Grover. Similar determinations by A. L. Davis[3] gave discordant results. As for isotopic lead its atomic weight is so variable as to show that it is nearly, if not always, a mixture of isotopes, and not a constant which can as yet be placed in the table. The values found have very great significance, but they are far from final.[4]

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[1] *J. chim. phys.*, 14, 389 (1916). See review by Guye in the same number, p. 361.

[2] *Ibid.*, 15, 293 (1917).

[3] *Ibid.*, 15, 334 (1917). Reiman and Murray assume H = 1.008; Moles prefers 1.0076.

[4] *Carnegie Inst. Pub.*, 267 (1918).

[5] *Compt. rend.*, 163, 415 (1916).

Gallium.—By the analysis of carefully purified gallium chloride, Richards, Craig, and Sameshima[5] find $Ga = 70.09$ and 70.11. These determinations, however, are only preliminary, but they justify the provisional adoption of the value 70.10. The original values given by the determinations of Lecoq de Boisbaudran vary from 69.70 to 70.12, the last one being very near the new value.

Zirconium.—From the ratio between zirconium chloride and silver, *Venable and Bell*[6] *find* $Zr = 91.76$. *Although this determination is re*garded as preliminary, the authors, by pointing out sources of error in all previous values, believe the new one to be the most probable. It seems best, however, to await the complete investigation before changing the value heretofore accepted.

Tin.—Baxter and Starkweather,[7] by electrolyses of stannic chloride, find $Sn = 118.703$ when $Cl = 35.457$. This is in complete agreement with Briscoe's determination, $Sn = 118.698$. The value 118.70 has already been adopted by the committee.

Tellurium.—Staehler and Tesch,[8] from careful syntheses of tellurium dioxide, find $Te = 127.51$, which is confirmatory of the accepted value 127.5.

Yttrium.—Hopkins and Balke,[9] by conversion of Yt_2O_3 into Yt_2Cl_3 find $Yt = 88.9$. The ordinary sulfate method is shown to be inaccurate. In a later investigation Kremers and Hopkins[10] determined the ratio between yttrium chloride and silver, and found $Yt = 89.33$. Since this method is the most trustworthy the value given by it should be adopted. The other sulfate determinations are questionable.

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[1] THIS JOURNAL, 38, 2613 (1916).

[2] *Ibid.*, 39, 537 (1917).

[3] *J. Phys. Chem.*, 22, 631 (1918).

[4] For discussions regarding the atomic weight of isotopic lead see the Presidential address of Richards before the American Association for the Advancement of Science in December, 1918. Also F. W. Clarke, *Proc. Nat. Acad. Sci.*, 4, 181 (1918).

[5] *Proc. Nat. Acad. Sci.*, 4, 387 (1918).

[6] THIS JOURNAL, 39, 1598 (1917).

[7] *Proc. Nat. Acad. Sci.*, 2, 718 (1916).

[8] *Z. anorg. allgem. Chem.*, 98, 1 (1916).

[9] THIS JOURNAL, 36, 2332 (1916).

[10] *Ibid.*, 41, 718 (1919).

Samarium.—The atomic weight of samarium has been determined by Stewart and James[1] from the ratio between the chloride and silver. The value found is 150.44, which is essentially that given in the table. No change is needed.

Dysprosium.—Engle and Balke,[2] by conversion of the oxide into the chloride, found Dy = 164.228. Later, by the same method, Kremers, Hopkins, and Engle[3] found Dy = 163.83. This discordance, like that already shown for yttrium, led the last named chemists to determine the ratio between dysprosium chloride and silver, which gave 162.52. The earlier method is discredited and the last value, rounded to 162.5, seems to be the one best entitled to acceptance.

Erbium.—For this element, by the oxide-chloride method, Wichers, Hopkins, and Balke[4] obtained values ranging from Er = 168.00 to 168.84. The method of determination is thus again shown to be untrustworthy.

Thorium.—In a long series of concordant analyses of thorium bromide, Hönigschmid[5] finds Th = 232.152 from the silver ratio and 232.150 from the silver bromide ratio when Br = 79.916. The value Th = 232.15 should be adopted for general use. He also studied thoria from uranium ores, which contained ionium. For this mixture he obtained an atomic weight slightly in excess of 231.50. This may approximate to the unknown atomic weight of ionium.

Uranium.—The latest series of determinations of the atomic weight of uranium by Honigschmid and Horovitz[6] was based like their earlier series upon analyses of the tetrabromide. Two sets of analyses were made, one upon a bromide which had been fused in bromine vapor, the other in nitrogen. The value obtained ranged from U = 238.04 to 238.16, the latter being in harmony with their former determinations. The rounded figure 238.2 is given in the table.

Helium.—Taylor,[7] using the microbalance for determining the density of helium, finds He = 4.0008. Guye,[8] in a recalculation of the data, finds He = 3.998. The value 4 should be retained.

Argon.—From the density and compressibility of argon, Leduc[9] finds A = 39.91. He regards the second decimal as uncertain, and advises the adoption of the rounded value 39.9.

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[1] THIS JOURNAL, 39, 2605 (1917).

[2] *Ibid.*, 39, 67 (1917).

[3] *Ibid.*, 40, 598 (1918).

[4] *Ibid.*, 40, 1615 (1918).

[5] *Z. Elektrochem.*, 22, 18 (1916).

[6] *Monatsh.*, 37, 185 (1916).

[7] *Phys. Rev.*, 10, 653 (1917).

[8] *J. chim. phys.*, 16, 46 (1918).

[9] *Compt. rend.*, 167, 70 (1918).

International Atomic Weights, 1920.

	Symbol	Atomic weight.		Symbol	Atomic weight.
Aluminum	Al	27.1	Molybdenum	Mo	96.0
Antimony	Sb	120.2	Neodymium	Nd	144.3
Argon	A	39.9	Neon	Ne	20.2
Arsenic	As	74.96	Nickel	Ni	58.68
Barium	Ba	137.37	Niton (radium emanation)	Nt	222.4
Bismuth	Bi	208.0	Nitrogen	N	14.008
Boron	B	10.9	Osmium	Os	190.9
Bromine	Br	79.92	Oxygen	O	16.00
Cadmium	Cd	112.40	Palladium	Pd	106.7
Caesium	Cs	132.81	Phosphorus	P	31.04
Calcium	Ca	40.07	Platinum	Pt	195.2
Carbon	C	12.005	Potassium	K	39.10
Cerium	Ce	140.25	Praseodymium	Pr	140.9
Chlorine	Cl	35.46	Radium	Ra	226.0
Chromium	Cr	52.0	Rhodium	Rh	102.9
Cobalt	Co	58.97	Rubidium	Rb	85.45
Columbium	Cb	93.1	Ruthenium	Ru	101.7
Copper	Cu	63.57	Samarium	Sa	150.4
Dysprosium	Dy	162.5	Scandium	Sc	44.1
Erbium	Er	167.7	Selenium	Se	79.2
Europium	Eu	152.0	Silicon	Si	28.3
Fluorine	F	19.0	Silver	Ag	107.88
Gadolinium	Gd	157.3	Sodium	Na	23.00
Gallium	Ga	70.1	Strontium	Sr	87.63
Germanium	Ge	72.5	Sulfur	S	32.06
Glucinum	Gl	9.1	Tantalum	Ta	181.5
Gold	Au	197.2	Tellurium	Te	127.5
Helium	He	4.00	Terbium	Tb	159.2
Holmium	Ho	163.5	Thallium	Tl	204.0
Hydrogen	H	1.008	Thorium	Th	232.15
Indium	In	114.8	Thulium	Tm	168.5
Iodine	I	126.92	Tin	Sn	118.7
Iridium	Ir	193.1	Titanium	Ti	48.1
Iron	Fe	55.84	Tungsten	W	184.0
Krypton	Kr	82.92	Uranium	U	238.2
Lanthanum	La	139.0	Vanadium	V	51.0
Lead	Pb	207.20	Xenon	Xe	130.2
Lithium	Li	6.94	Ytterbium (Neoytterbium)	Yb	173.5
Lutecium	Lu	175.0	Yttrium	Yt	89.33
Magnesium	Mg	24.32	Zinc	Zn	65.37
Manganese	Mn	54.93	Zirconium	Zr	90.6
Mercury	Hg	200.6			

In the above table of atomic weights proposed for 1920, few changes have been made from the values given in the last preceding table. The new values are A = 39.9; B = 10.9; Ga = 70.1; Th = 232.15; and Yt = 89.33. In addition to these the atomic weight of nitrogen should be changed from 14.01 to the more precise value 14.008. The latter figure represents all the best determinations, and is probably correct to within 1 in the third decimal place. For so small a value the change is insignificant.

Signed F. W. CLARKE,
T. E. THORPE,
G. URBAIN.

[CONTRIBUTION FROM THE ELECTROCHEMICAL LABORATORIES OF THE UNIVERSITY OF MANCHESTER.]

THE OCCLUSION OF HYDROGEN AND OXYGEN BY METAL ELECTRODES.

Criticism of the Paper by Harding and Smith.[1]

BY EDGAR NEWBERY.

Received May 26, 1919.

The very careful work and ingenious apparatus of Harding and Smith call for some remarks of appreciation; and at the same time the theory of conducting hydrogen as developed by them appears to be open to doubt. The following comments are not offered in any spirit of carping criticism, but rather with the thought of friendly collaboration and interchange of views, and the object of reaching the real truth underlying some very interesting phenomena.

When a current is first passed through an electrolytic cell containing a palladium cathode in dilute acid, hydrogen ions are discharged upon the cathode surface and the monatomic hydrogen thus formed is at once absorbed by the metal, being kept in the monatomic form by the dissociating action of the solvent metal. This hydrogen will gradually diffuse to the interior of the metal, and, since the solution has a lower conductivity than the pure metal, the electric resistance of the metal will rise.

After a comparatively short time the external layers of metal will become saturated with hydrogen and the single potential of the metal solid solution will be that of a hydrogen electrode. Hydrogen ions, on discharging, will now no longer disappear into the metal but will tend more and more to stick on the outer surface, being held there by electrostatic forces, thus insulating the outlying parts of the electrode. New ions must therefore penetrate farther and farther into the surface before they can discharge. These ions are again followed by others which arrive faster than the discharged ions can collect together to form molecules, and consequently "blocks" will occur in the large crevices (large compared with an ion) in the metal surface. Since these latest arrivals carry electric charges opposite in sign to the charge on the electrode and are separated from the electrode only by the diameters of two or three atoms or molecules, inconceivably great pressures are set up which may easily attain a magnitude of 10^{80} atmospheres close to the outer surface. These pressures are logarithmically proportional to the potential differences between the two attracting surfaces and will therefore be greatest near the solid-liquid boundary; but since the gas diffuses slowly to the interior of the metal increasing the resistance all the way, there will be a small fall of potential from the surface to the inner core of the palladium and consequently a gradually decreasing pressure extending an appreciable distance into the metal. The effects produced will therefore be more noticeable in fine wires or thin sheets than in thicker ones.

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[1] THIS JOURNAL, 40, 1508 (1918).

When very low current densities are employed, the above description will hold good. With higher current densities, however, a new set of phenomena appears. The pressures now become so great that the hydrogen is forced into actual combination with the metal, producing hydrides. These hydrides conduct like a metal and ionize like a metal, and their high solution pressures give rise to the excess back e. m. f. known as overvoltage.

When the current is interrupted, the external pressure is at once released. Immediately, therefore, the excess gas dissolved in the metal will tend to come out of solution, expanding the metal and making it spongy, thus increasing its resistance rapidly at first and more slowly afterwards. At the same time, the hydrides formed, which are only stable under high pressures, decompose and intensify the above effect. The consequence of this liberation of gas from within the metal will be that a series of small craters will be blown in the surface of the metal and these craters are easily visible under the microscope not only in the case of palladium, but with every metal so far experimented with.

Since there is good evidence, from overvoltage work, that the hydrides are good metallic conductors, it is probable that the disappearance of these will further increase the resistance of the metal, as the whole would conduct better when the pores are filled with conducting hydride under pressure than when filled with gas.

When a considerable quantity of gas has escaped, the internal strains in the metal will be released and the metal will gradually recover its original texture, the walls of the cavities filled with gas will fall together as the gas escapes, and the resistance of the metal will again fall. On heating and annealing, the metal will return completely to its original condition, provided the evolution of gas has not been so violent as to distort the surface permanently.

Changes of Length.

If the cathode is a palladium wire, changes of length occur (1) due to solution of hydrogen in the metal; (2) due to formation of hydride. Since the application and release of pressure occurs laterally and chiefly in the outer layers of the wire, the central core may be but slightly affected and will tend to hold the outer layers in position, thus masking the effect except with very fine wires. The change of length is therefore not a satisfactory guide to change of volume except in special circumstances. It might be expected that the formation of a solid hydride would have a greater expanding effect than the absorption of gas, and this is supported by the experimental evidence of Thoma and Fischer.[1] Since the quantity of hydride formed is dependent upon the current density, a definite length should correspond with each current density when equilibrium has been attained. Further, since the replacement of gaseous hydrogen by solid hydride diminishes the resistance of the metal, there should be an inverse relationship between resistance and length under these equilibrium conditions. This has been well established experimentally, as described in the paper under discussion.

Finally, the typical experiment curve,[2] Fig. 2, may be described as follows:

A to B.—Absorption of hydrogen with production of solid solution having higher resistance than pure metal. Metal becomes spongy.

B to C.—Formation of hydride which fills some of the cavities originally occupied by gas, thus reducing resistance.

C to D.—Release of external pressure resulting in spontaneous decomposition of hydride, and escape of gas internally, rendering metal still more spongy, and therefore of still higher resistance.

D to E.—Escape of gas externally, due to bursting of surface. Walls of cavities fall together and reduce resistance.

E to F.—First application of external pressure produces still closer conjunction of walls of cavities and rapid fall of resistance.

F to G.—Reabsorption of gas. Since passages have now been formed in the metal, this occurs much more rapidly and completely than in the first instance.

G to I.—Renewed formation of hydride. This will also occur more rapidly than before due to the existence of ready-made passages into the interior of the metal.

I to J.—Rapid expansion of cavities due to release of external pressure. More rapid than previously owing to weakening of external cohesive forces by the treatment undergone.

J to K.—Complete removal of gases and collapse of cavities.

The quantity of hydride produced appears to be dependent upon the current density though it is not proportional to the current density. Hence, for a given current density, the equilibrium stage attained will be approximately the same whatever the previous treatment.

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[1] M. Thoma, *Z. physik. Chem.*, 3, 69 (1889); F. Fischer, Drude's *Ann.*, 20, 503 (1906).

[2] *Loc. cit.*, p. 1513.

Briefly, my doubts of the "conducting hydrogen" theory are based upon a quantitative view of the effects produced. It appears certain that up to saturation point the hydrogen dissolved in palladium is very largely composed of atomic hydrogen, probably over 80%. This atomic hydrogen is responsible for the single potential of the hydrogen electrode, and if a metal is incapable of dissociating hydrogen in this way, it cannot be used in the construction of a hydrogen electrode. The addition of more hydrogen (supersaturation), one would expect would tend to diminish the total percentage of atomic hydrogen by bringing the atoms into closer proximity, just as a concentrated salt solution is less dissociated than a dilute.

The fact that up to saturation point the resistance of palladium is greatly increased by the inclusion of hydrogen (most of which is in the atomic state), renders it improbable that the addition of further hydrogen in the atomic state will decrease this resistance.

The action of the added hydrogen would not alter the single potential of the electrode. But experiment shows that under certain conditions the single potential of the palladium electrode takes a sudden leap to a much higher value, nearly 0.7 volt above the hydrogen electrode, and this same value is also shown under similar circumstances by nearly every metal capable of acting as a divalent metal in compound formation. This evidence, together with other which could be cited if necessary, is almost overwhelming in support of the view that a definite hydride is now formed in the metal. It must therefore be taken as proved that hydrides do exist in the metal under these conditions, although the question as to whether they are responsible for the changes of electrical resistance observed in palladium is still open.

The hydrides thus formed are stable only under the great electrical and mechanical stresses present at the time of their formation, and up to the present none of this special type of metallic hydride has been isolated. Nevertheless, it is possible to predict their properties with comparative certainty by analogy with many oxides produced under almost identical circumstances. Some of these oxides, lead dioxide, manganese dioxide, etc., are easily isolated and their properties well known. The property which specially concerns us here is their electrical conductivity, which is considerable, though far below that of the metal itself. Since the hydrides show so many properties in common with these oxides, it is only reasonable to consider that they have a quite appreciable electrical conductance. Further, if they form solid solutions in the metal, such a solution is likely to be a better electrical conductor than a solution of gaseous hydrogen in the same metal.

Whether, therefore, the hydrides form solid solution with the metal, or whether they merely fill cavities in the metal formerly occupied by gas, their appearance will be demonstrated simultaneously by a fall in the electrical resistance of the metal and by a rise in the (negative) single potential.

The accuracy with which the experimental wire recovers its original resistance when very carefully treated is at first sight puzzling, but on further examination becomes not only reasonable but gives us further interesting information as to the processes going on during formation of the hydrides.

It is well known that all metals in the massive state consist of crystals cemented together by amorphous material. This amorphous material is not, strictly speaking, a solid but a highly viscous liquid, and many of the mechanical and physical properties of the metals are due to this substance which forms an envelope for every crystal of the metal. Polishing the metal consists in pressing down the metallic crystals and smoothing over this liquid on the top. Since palladium is easily brought to a state of brilliant polish, it is probable that the amorphous material is fairly plentiful in this metal. It also appears probable that colloidal palladium and the amorphous metal have much in common even if they are not identically the same. The great so-called "catalytic" power of colloidal palladium is well known and appears to be due to its great dissolving and dissociating power for gases like hydrogen. It appears, therefore, that the solution of hydrogen in palladium is due mainly (possibly wholly) to the amorphous or liquid part of the metal, and further, that the hydrides are formed from the same substance. This substance, therefore, being a liquid, cannot have its shape destroyed, and if it is merely expanded and afterwards contracted again without any violent disturbances occurring sufficient to displace the crystals permanently, there is no reason why the final properties of the body as a whole should be different from the initial properties.

The greater solubility of hydrogen in the amorphous phase is observable in other metals than palladium, *e. g.*, the embrittling and hardening of iron after use as a cathode, is due to the weakening of the cohesive power and increase of viscosity of the amorphous binding material by solution of hydrogen and possibly, also, to the formation of minute crystals of solid hydride.

The observations under discussion, therefore, are of great interest in showing that both solution of hydrogen and hydride formation in palladium are almost entirely due to the action of amorphous or liquid palladium, the solid crystals taking little or no part in the process.

The application of the phase rule to this problem is very unsafe since we are dealing with a system highly heterogeneous and not in equilibrium. Even under the conditions represented by horizontal lines on the diagram in the paper under discussion, true equilibrium is not present since we have irregularly decreasing mechanical pressures and electrical stresses as we proceed from the surface of the wire to the internal core. If any attempt be made to apply the phase rule to this state, then these variable pressures must be considered in the character of new components, and since the pressures vary indefinitely, the number of phases possible is also indefinite.

MANCHESTER, ENGLAND

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF PRINCETON UNIVERSITY.]

THE OCCLUSION OF HYDROGEN AND OXYGEN BY METAL ELECTRODES.

Comment on Newbery's Criticism.

BY EARLE A. HARDING AND DONALD P. SMITH.

Received May 26, 1919

The foregoing interpretation of our results, in terms of Professor Newbery's hypothesis of unstable hydrides, to which he has been led by extensive studies of overvoltage, involves several questions of wide bearing. We shall in the main confine ourselves, however, to pointing out difficulties which attend the explanation of our own observations in the manner suggested, and commenting on the objections raised with regard to "conducting hydrogen."

Since the conduction of a platinum wire cathode has been shown to rise above that of the unaffected metal,[1] it would, in this instance at least, be necessary to attribute to the supposed hydride a volume conductivity greater than that of its metallic component, and hence of a higher order than any hitherto observed for compound or solid solution. The same applies to the oxide which must logically be assumed to account for the analogous effect found with a palladium anode.[2] If compounds, whether formed in fixed or in variable proportions, afford the explanation, they must therfore belong to a new category having extraordinary electrical characteristics.

The changes of resistance exhibited by the cathodes when electrolysis is renewed after temporary interruption, consist in three parts: a very rapid initial drop (seen in Curves 1, 2 and 3 of Fig. 6, of the original article, in the enlarged reproduction of No. 1 given at the lower left side of the same figure, and at E–F in Fig. 2); a subsequent rise to the maximum; and a final decline to the steady value determined by the current density. It is not readily apparent why the formation of the supposed hydrides, stable only at very high pressures, should be most in evidence in the first stage of this occlusion, when electrolysis has just begun and the pressure of hydrogen within the electrode must be relatively low. Nor does it seem

[1] THIS JOURNAL, 40, 1530 (1918).

[2] *Loc. cit.*, Fig. 8, p. 1524, *et seq.*

to follow from the hydride hypothesis, without the addition of special assumptions, that the production of hydrides should predominate during the first and last stages, while formation of solid solution prevails in the intermediate part of the process.

The initial drop of resistance, just mentioned, is attributed by Professor Newbery to "closer junction of the walls of cavities," implying a contraction of the wire. It was perhaps not made plain that the falling first portions of the curves of Fig. 4*a* represent the ends of the evolution curves, and that the length of the wire, in these and in all our experiments, *increased* instantly upon renewal of electrolysis. During the drop of resistance from E to F the wire is therefore expanding; and for this the hydrides do not seem to offer a ready explanation.

The assignment of the supplementary conductance to hydrides seems also unadapted to account for the initial drop of resistance observed when a wire previously subjected to oxidation is made to serve as cathode (*loc. cit.*, middle of p. 1525), and the absence of this drop when unoxidized wires are employed. Any effect left by oxidizing influences must be of a kind to delay, rather than to hasten, the attainment of high hydrogen pressures, and hence must operate in the earlier stages of electrolysis to diminish the quantity of hydrides, if these are stable only at high pressures. The consequence of oxidation should, therefore, be the opposite to that found.

Turning to Professor Newbery's objections to the supposition of a conducting form of hydrogen, we may point out that his statement that "the addition of more hydrogen (supersaturation), * * * would tend to diminish the total percentage of atomic hydrogen by bringing the atoms into closer proximity, just as a concentrated salt solution is less dissociated than a dilute," overlooks the fact that an electrode, during the persistence of the supplementary conductance, is not yet in a state of equilibrium; and that the analogy is not to an electrolyte to which more ionogen is added, but rather to a slowly reacting mixture, into which is rapidly introduced an excess of one of the reactants It is evident that in such a case the added factor (and any intermediate product), would be present in more than equilibrium proportion until the end state had been reached.

We are unable to see the force of the objection that "the fact that up to saturation point the resistance of palladium is greatly increased by the inclusion of hydrogen (most of which is in the atomic state), renders it improbable that the addition of further hydrogen in the atomic state will decrease this resistance." This appears to us to be fully met by the consideration set forth in the paper under discussion (p. 1518, *et seq.*).

Nor can we agree that "the action of the added hydrogen would not alter the single potential of the electrode." It appears to us almost inevitable that the accumulation of a transient intermediate form within the metal should raise the electrolytic solution pressure of hydrogen.

While we would not deny the possibility that Professor Newbery's explanation may be the correct one, we must therefore still regard our own as involving a less sweeping and more definite assumption. A metallic compound, existing within an alloy side by side with a solid solution from which it differs diametrically in properties, but from which it does not form a distinct phase, constitutes something new to metallography; and the novelty of the conception is not diminished by supposing both solid solution and compound to form part of an amorphous cement, the existence of which is itself by no means universally admitted. The unique electrical properties with which the compound must further be endowed, add to the scope of the assumption.

On the other hand, to suppose that the hydrogen (or oxygen) which has yielded its charge to the electrode and penetrated the latter, not improbably in a monatomic condition, is capable of again receiving charges from the metal and transporting these charges under the influence of the potential gradient associated with the measuring current, appears to imply nothing new save, perhaps, the conception that the hydrogen retains its mobility after entering the metal until it enters into the close chemical relationship of the solid solution, or as otherwise transformed; and for this conception the behavior of the palladium wires appears to us to afford strong support not only in the changes of length, but in the disruptive effect produced when hydrogen-filled wires are quickly raised to a temperature above the critical point at which a rapid fall of resistance occurs (bottom of p. 1510, *et seq.*). This seems to indicate very clearly that at this temperature the solid solution releases hydrogen into a mobile form which exerts great internal pressures.

The conception makes at present no pretense of being more than a working hypothesis. As such it has the advantage of being quite definite, and hence suggesting many questions of fact. Since some of these are at present the subject of experiment, further elaboration of our point of view may appropriately be deferred.

PRINCETON, N. J.

[CONTRIBUTION FROM THE ELECTROCHEMICAL LABORATORIES OF THE UNIVERSITY OF MANCHESTER.]

REPLY TO HARDING AND SMITH'S COMMENTS ON NEWBERY'S CRITICISM.

BY EDGAR NEWBERY.

Received October 7, 1919

The most important objection raised by Professor Smith and Dr. Harding to my suggestion that the overvoltage hydrides and higher oxides are responsible for the changes of electrical resistance observed by them, lies in the supposition that these compounds have a higher electrical conductivity than has the metal itself. Personally, I do not believe that such conductivity of compounds is possible and I am unable to agree with the above authors that the postulation of this high conductivity is at all necessary.

The first application of a potential difference between the wire and the surrounding medium produces an electrical double layer which must exert enormous mechanical pressure upon the outer layers of the wire. This pressure will not only close up some of the cavities already formed in a previously treated wire, but will even compress the crystals of an untreated wire into closer contact, thus increasing the conductivity. This lateral pressure on the wire would naturally tend to increase its length, which is in accordance with the observations of Harding and Smith.

In the case of palladium the rate of absorption of hydrogen is so rapid that this initial increase of conductivity is not observable with an untreated wire, although it is readily observed when oxygen is liberated. Hydride formation does not occur until after the surface is saturated with dissolved hydrogen.

This "electro-striction" effect is quite outside the hydride hypothesis and occurs before hydrides have time to form. This, perhaps, meets the objections raised by Professor Smith amd Dr. Harding in the first 4 paragraphs of the preceding paper. The fall of resistance referred to in the fifth paragraph is evidently due to the rapid reduction of oxide to metal.

My most serious objection to Smith and Harding's theory may be stated bluntly as follows: If 80 cc. of atomic hydrogen introduced into metallic palladium increases its resistance to a degree roughly proportional to the quantity of gas absorbed, why should a further 20 cc. of the same gas reduce the resistance? My belief is that the last 20 cc. does not exist in the form of gas, but is chemically combined with the palladium and this belief is based on the fact that its electrolytic potential is widely different (up to 0.7 volt) from that of the 80 cc. of monatomic hydrogen first introduced. Smith and Harding's theory entirely fails to account both for the constancy of the potential up to this point and for this sudden and very great change in electrolytic potential which occurs simultaneously with the fall of resistance. The mere accumulation of an extra 20% of a gas already present is quite inadequate to explain this. Also, the fact that the voltage attained is determined by the valence of the metal can hardly be reconciled with any theory which does not involve chemical compounds.

To test my views of the possibility of electro-striction affecting the resistance of the wire I would suggest that Prof. Smith and Dr. Harding should make the following simple experiment which I am unfortunately unable to make for myself at the present moment: A long, fine wire of platinum or palladium should be coiled closely round a mica plate (a platinum resistance thermometer would do very well) and its resistance measured when immersed in various electrolytes—pure water, strong acid or alkali, and also in oil or benzene, as well as in air.[1]

One important point has been overlooked in the original experiments of Smith and Harding, namely the conductivity of the electrolyte. In their apparatus this is certainly appreciable and the highly complicating phenomena of transfer resistance are also present. A certain quantity of current must of necessity flow through the electrolyte alongside the wire. If the resistance of the circuit, wire-electrolyte-wire, were constant, the shape of the curves would be unaffected. Unfortunately, this is far from being the case. The transfer resistance opposing the passage of current between the wire and the electrolyte is a quantity which varies according to circumstances from 0 to over 1000 ohms per sq. cm., and the lower this transfer resistance, the greater the current carried by the electrolyte. It is quite impossible to predict what this transfer resistance will be, since it is dependent upon temperature, current density, time, material and condition of electrode, electrolyte, and specially upon the previous history of the electrode, and its variation is not regular with any of these quantities or qualities. The confusion introduced by this troublesome factor is great enough to invalidate both of the explanations suggested for Harding and Smith's observations, and its elimination promises to be equally troublesome. Experiments with very wide and very narrow tubes surrounding the wire and also with electrolytes of varying conductivity might indicate what allowances should be made. It is possible that with a very narrow surrounding tube and an electrolyte of high resistance, some features of the curve may tend to disappear. If so, these features may be safely put down to transfer resistance. Until some such experiments on these or similar lines have been carried out, it is perhaps unwise to attempt any further explanation of the observed phenomena.[2]

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[1] This form of experiment is of course open to the same objections as those mentioned in the following section. Nevertheless it is worth trying.

[2] An account of transfer resistance may be found in *J. Faraday Soc.*, 15, I (1919), "The Resistance of an Electrolytic Cell."

One further point may be mentioned with regard to the ninth paragraph of Harding and Smith's comment on my criticism. They refer to "a metallic compound existing within an alloy side by side with a solid solution from which it differs diametrically in properties, but from which it does not form a distinct phase."

I agree that such a hypothesis is very improbable and I had no idea of suggesting this. Though the application of the phase rule to such a system which is not in equilibrium is very unsafe, yet if we consider a very small volume in the interior of the metal where the changes are progressing slowly, the condition of equilibrium may approximately hold.

We have two components, metal and monatomic gas. Metal may be considered to have ceased to exist as pure metal and the phases present will be saturated solid solution, metallic hydride, free gas. If the pressure be increased, more gas will combine with the solid solution to form hydride If it be decreased, hydride will decompose giving free gas and solid solution. The hydrides, therefore, form a distinct phase with a definite dissociation pressure for a given temperature, the whole process being exactly analogous to the decomposition of calcium carbonate by heat. The fact that hydrides are actually formed hardly admits of dispute, the evidence being almost overwhelming,[1] while the formation of the corresponding oxides is a well established fact. The question at issue is not whether these compounds exist, but whether they are responsible for the resistance changes observed by Harding and Smith.

In conclusion, I desire to express my appreciation of the courtesy and broad-mindedness with which Professor Smith and Dr. Harding have met my criticisms and also my admiration of the delicacy and ingenuity of their apparatus and the work under discussion.

MANCHESTER, ENGLAND

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF PRINCETON UNIVERSITY.]

COMMENT ON PROFESSOR NEWBERY'S REPLY.

BY EARLE A. HARDING AND DONALD P. SMITH.

Received October 7, 1919.

The first new explanation advanced in this reply assumes that the resistance of the palladium wire is reduced by an electrostrictive effect. Since, at 25°, the average pressure coefficient of the resistance of palladium[2] is only -0.1887×10^{-6}, the electrostriction necessary to cause a change of resistance of 25% would be of a magnitude far beyond any which could be produced by the small voltages applied (<6 volts). Moreover, this explanation assumes that the crosss section of the wire is reduced during the occlusion of hydrogen, whereas the reverse is the case. Occlusion is accompanied by expansion in all directions.[1]

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[1] See *J. Chem. Soc.*, 109, 1051, 1066, 1107, 1359 (1916); 111, 470 (1917); also *Manchester Memoirs*, 61, No. 9 (1917).

[2] Bridgman, *Proc. Am. Acad.*, 52, 612 (1916).

Another explanation offered is that a shunt conduction through the electrolyte, by which the wire was surrounded, varied with the transfer resistance between wire and electrolyte, and that these variations were responsible for the changes of resistance observed. Such an explanation is clearly inapplicable to the experiments in which the supplementary gain of resistance was found to continue unaltered after the electrolyte had been withdrawn.[2] In the ordinary experiments, each wire was annealed to constant resistance in nitrogen, and its resistance was again taken after the introduction of the electrolyte, but before electrolysis was begun. In no instance could a change of resistance, due to the presence of the electrolyte, be detected with certainty. Hence the shunt conduction was itself negligible, and such second-order differences in this factor as may have resulted from changes of transfer resistance could hardly have exerted an appreciable effect. It should be borne in mind that our measurements of resistance were not made while the electrolytic current was flowing.

As regards Professor Newbery's further elucidation of his hydride explanation, it does not appear to us in any way to remove the necessity for attributing to these compounds the extraordinary conductivities discussed above.

We are, therefore, still of the opinion that the simplest explanation of the supplementary conductance is to be found in the assumption of a transient conducting form of hydrogen.

PRINCETON, N. J.

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF ILLINOIS.]

THE ELECTROLYTIC DETERMINATION OF THE HALOGENS: AN INDIRECT METHOD.

BY J. H. REEDY.

Received June 2, 1919.

The determination of the halogens by their electrolytic deposition on silver anodes has been regarded by most investigators as impracticable, since the silver anode begins to dissolve, either during the last stages of the electrolysis, or immediately upon completion of the halide ion deposition. Results are low, owing either to precipitation of silver halides in the solution or to the migration of silver to the cathode. Various expedients to overcome this difficulty have not proved satisfactory, and gravimetric and volumetric methods have remained the standard processes for these determinations

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[1] Poggendorff, *Phil. Mag.*, [4] 37, 474–5 (1869); Thoma, *Z. physik. Chem.*, 3, 71 (1889).

[2] THIS JOURNAL, 40, 1516 (1918).

In a previous paper[1] it was shown that in most solutions there is a retardation in the solution of silver anodes until an anodic potential of about 0.52 volt[2] is reached, when the current, which is analytically negligible below this value, rather abruptly shows a marked acceleration of action. With halide solutions, however, action begins at lower potentials, depending upon concentration. The relation between potential and concentration is shown in Fig. 1. This suggests that the deposition of the halogens might be accomplished by carrying out the electrolysis with an anode potential of 0.52 volt, or a very slight excess of this value. To this end the decomposition potential of a 0.5 molar sulfuric acid solution saturated with silver chloride was determined, using silver coated with silver chloride as an anode and bright platinum as the cathode.

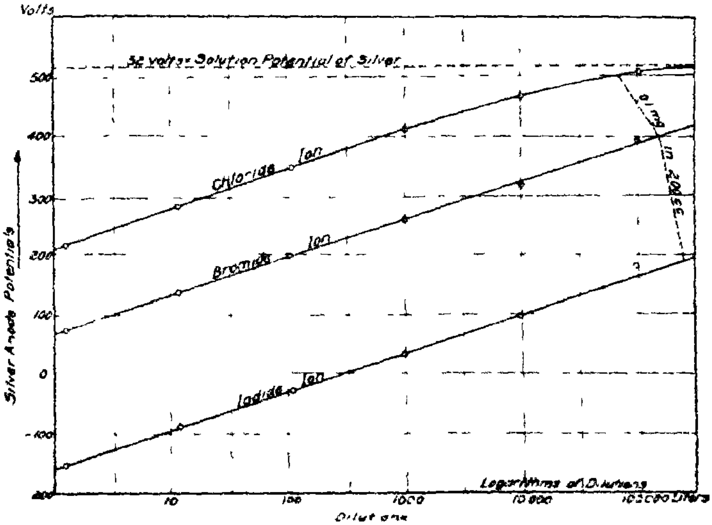

Fig. 1.—The change of potential of silver halide electrodes with dilution of ions.

This value was found to be 0.59 volt, which corresponds exactly with the "solution potential" of silver (0.52 volt) plus the overvoltage of hydrogen upon bright platinum (0.07 volt). As long as this limiting voltage of 0.59 is not exceeded, the electrolysis of halide solutions with silver anodes was found to proceed with the formation of an adherent layer of silver halide on the anode and without precipitation in the solution. With the completion of the deposition of the halide ions, silver ions appeared in the solution with no break in the continuity of the current and with a scarcely noticeable rise in potential.

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[1] *Am. J. Sci.*, 40, 400 (1915).

[2] Referred to the normal hydrogen electrode as 0.0 volt

In order to maintain the conductivity of the electrolytic solution, especially at low concentrations of the halogen ions, some "inert" electrolyte must be present. Since there is a tendency towards increasing alkalinity in all electrolytic solutions where hydrogen is liberated at the cathode and the anion discharged is not hydroxyl, neutral solutions are not favorable media for this operation. The reaction potential of hydroxyl ions on silver anodes is only slightly above that of chloride ions, and with the increase in concentration of the former the potential is reached where hydroxyl ions will be discharged more readily than chlorine ions. Under such circumstances the deposition of the halogen can never reach completion. For this reason, in the experiments reported below, the halides were electrolyzed in the presence of 0.5 molar sulfuric acid.

It thus appears that the unsatisfactory technique of the usual methods for the electrolytic determination of the halogens may be much simplified and the process made more or less automatic by carrying out the analysis under a constant potential of 0.59 volt, and determining the halogen by loss of weight upon electrolytic reduction of the halide deposit to metallic silver. This indirect method is necessary since varying amounts of silver dissolve at the end of the electrolysis.

The apparatus is shown diagrammatically in Fig. 2. A lead accumulator, L, of fairly large capacity was used as a source of current, since this form of battery maintains an approximately constant potential on a closed circuit. The cathode was of bright sheet platinum, and the anode consisted of a frame of heavy silver wire covered with a cylindrical surface of fine silver gauze, the whole being coated with silver electrolytically, and afterwards heated in an electric oven to make the deposit firm and adherent. The volume of the electrolyte used was 200 cc. The voltage was read from a voltmeter, V, connected as shown in the figure, so that any current passing through it would not be indicated by the milliammeter M. By means of the sliding resistance R the potential was set at 0.59 volt. Upon closing the circuit a rather large current passed at first, but with the aid of efficient stirring diminished very rapidly and became negligible at the end of 15 minutes. The potential was then raised to 0.60

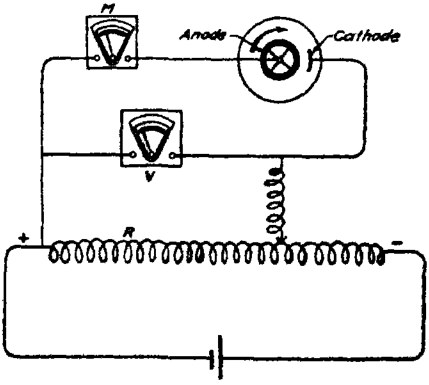

Fig. 2.—Diagram of apparatus

volt and the current pssed 5 minutes more. The silver electrode, with its halogen deposit, after weighing, was made the cathode in a dilute solution of sodium hydroxide, which was electrolyzed until hydrogen was formed freely upon the surface of the silver. The silver halide was thus reduced to black silver, which was not very adherent and had to be handled carefully to avoid loss. After thorough washing, the electrode was heated to about 500° in an electric furnace until the deposit was white and thoroughly sintered together. The loss in weight on reduction represents the weight of the halogen. In most cases more or less silver dissolves from the anode towards the end of the electrolysis, remaining in solution as silver sulfate or plating out on the cathode as metallic silver. Representative results are given in Table I.

TABLE I – DETERMINATION OF HALOGENS.

Wt of electrode + halogen G	Wt of reduced electrode G	Difference G	Error G	Wt of silver dissolved G
Chlorine Calc wt 0 0177 g				
21 1048	21 0873	0 0175	-0 0002	0 0007
23 2998	23 2823	0 0175	-0 0002	0 0050
23 2987	23 2804	0 0183	+0 0006	0 0019
23 2929	23 2736	0 0183	+0 0006	0 0068
23 1783	23 1608	0 0175	- 0 0002	0 0002
23 1443	23 1272	0 0171	-0 0006	. .
23 1432	23 1260	0 0172	—0 0005	0 0012
Bromine. Calc wt 0 0396 g				
21 1542	21 1145	0 0397	+0 0001	0 0011
21 1538	21 1144	0 0394	−0 0002	0 0071
21 1540	21 1144	0 0396	.	......
21 1389	21 0993	0 0396	. .	0 0151
21 1366	21 0968	0 0398	+0 0002	0 0025
23 2888	23 2492	0 0396	. . .	......
Iodine. Calc. wt 0 0629 g				
21 1777	21 1156	0 0621	+0 0001	......
21 1585	21 0966	0 0619	—0 0001	0 0002
23 3350	23 2729	0 0621	+0 0001	0 0006
23.3327	23 2708	0 0619	—0 0001	0 0021
23 3309	23 2691	0 0618	—0 0002	0 0017
23 3312	23 2628	0 0628	+0 0008	0 0063

From this it appears that, even in the case of chlorine, where the potential required for the complete deposition lies very close to the solution potential of silver the silver does not begin to dissolve until the precipitation of the halide is practically complete. It was found that, by carefully observing the limiting value, the formation of silver precipitates in the solution could be avoided. In a few cases, however, after the characteristic opalescence of the colloidal silver halide precipitate had appeared, it was found that by lowering the potential below 0.59 volt the solution could be cleared up again. But in cases where appreciable amounts of the silver halide had appeared in the solution, it was coagulated by the stirring, and in such form it dissolves too slowly for electrolytic decomposition to be practicable.

In spite of the unusual technique of the method, this procedure has been found to compare favorably with other gravimetric methods, both as to accuracy and speed. However, it must be confessed that this work was undertaken not so much for the purpose of developing a new method as for the confirmation of certain inferences drawn from the results of my study of electrode potentials.

URBANA, ILLINOIS.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF WASHINGTON.]

PASSIVITY OF COBALT.

BY HORACE G BYERS AND CURTIS W. THING.

Received June 5, 1919

Introduction.

In a paper by one of us[1] a report is given on a series of experiments on the passivity of cobalt and the following statement is made: "In solutions of the halogen salts, sulfates, nitrates, chlorates, nitrites, dihydrogen phosphate, citric acid, acetic acid, sulfuric acid, and nitric acid, cobalt as an anode goes quantitatively into solution. In the free acids, also, the metal dissolves by direct action of the acid so that the anode loss is greater than the copper equivalent. In caustic potash, neutral sodium carbonate, and potassium bichromate, cobalt fails to go into solution even to a minimal degree. When the plates which have been used in caustic potash are placed as anodes in solutions in which they dissolve, the initial high potential fall indicative of passivity is observed, provided the circuit is closed by immersion of the cobalt anode." It is stated in the contribution of Hollis[2] that cobalt, nickel and iron are passive in fuming nitric acid below a certain critical temperature which he fixes for iron at 100°, for nickel at 80° and for cobalt at 10°. In view of this contradictory behavior of cobalt and the difference between its behavior and that of iron and nickel it seemed worth while to make a further study of the topic. The experimental work detailed below is divided into 3 parts: (1) a study of the anodic behavior of cobalt in various solutions with change in concentration using small current density, (2) a study of the relation between the current density and the voltage drop across a platinum-cobalt cell using various solutions, and a comparison with similar cells using iron and nickel, and (3) a study of the anodic potentials of cobalt, iron and nickel.

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[1] THIS JOURNAL, 30, 1728 (1908)

[2] *Trans. Camb. Phil. Soc.*, 12, 462 (1904).

I.

The pure cobalt, in plate form of known area, was fastened to a copper conducting wire. This was, in turn, fastened in a glass tube and sealing wax applied so that the electrolyte came in contact with the cobalt only. The whole was suspended in a porous cup within a beaker and both were filled with the electrolyte. The cathodes used were two platinum wires, sealed through glass tubes, and were hung parallel to and at equal distances from the anode, on the outside of the porous cup. The cup served to keep the cobalt anode unaffected by the hydrogen from the cathodes. The two cathodes gave a more uniform current density on the anode The temperature used in all measurements was 0°.

The amount of solution from the anode was measured from the loss in weight of the anode during the passage of the current. From the copper deposited in a copper coulometer the amount of cobalt which would have dissolved, assuming the metal to dissolve in the bivalent condition and to conform to Faraday's laws, may be calculated. Comparing the amount actually dissolved to the amount which theoretically should dissolve, the degree of passivity was calculated

Except where otherwise indicated, the cobalt used was prepared electrolytically from nickel-free cobalt sulfate. A part of the work was done with Merck's 98% cobalt. No difference between the behavior of the two samples could be detected.

A. Nitric acid solutions of normality 0.01 to 5.0 were used. The current densities employed varied from 3.0 to 0.1 amp. per sq. dcm.

B. Sulfuric acid solutions of normality 0.02 to 5.0 were used. The current densities employed varied from 0.1 to 2.7 amp. per sq. dcm. With these current densities the cobalt was active. In every case the cobalt went into solution in accord with Faraday's law plus an amount varying between 9 and 110%, due to the solvent effect of the acid. The metal was evidently active.

It was afterwards found that in a 0.2 *N* solution, if the current density was increased to 16–17 amp. per sq. dcm. and then reduced to the densities noted in Table I, that the cobalt would be passive. This is shown in the following table:

TABLE I.—98% COBALT IN 0.2 *N* SULFURIC ACID AT 0°.

Area anode Sq. cm.	Current Mil. amp.	Loss of anode G.	Gain of copper G.	Current density Amp. per sq. dcm.	% loss of anode
0.256	10	0.0100	0.0105	3.92	100.3
0.330	15	0.0151	0.0158	5.0	102.0
0.272	15	0.0004	0.0187	5.5	2.3
0.322	15	0.0002	0.0207	4.6	1.0

In the first two cases the initial high density was not employed and the cobalt was active. In the last two cases the initial high current density of 16–17 amp. per sq. dcm. rendered the cobalt passive and it remained passive even at the low current densities of 5.5 and 4.6 amp. per sq. dcm. The small loss was due to the initial period of activity and to mechanical losses during the cleaning and weighing of the electrode.

C. Sodium sulfate solutions of normality 0.01 to 5.0 were used. At small current densities the cobalt was active. Using 0.2 *N* solution, it was found that cobalt would become passive providing a sufficiently high current density as employed.

D. In potassium dichromate solutions of all concentrations and at all current densities cobalt remained passive. It was found that additions of small amounts of sulfuric acid or sodium sulfate solutions would render the cobalt active.

Summary.—In 0.2 *N* sulfuric acid and sodium sulfate solutions, cobalt may be either active or passive at 0° dependent upon the current density. In potassium dichromate it readily assumes the passive state under all conditions. The passive state is not so readily reached in the presence of activating agents.

II.

A cell containing the electrolyte, having an anode of known area and a platinum foil cathode, was placed in series with a milliammeter. A voltmeter was connected across the two electrodes by means of a key. In series with the cell and ammeter was a variable resistance. A direct current of 15 volts was used.

The voltage fall across the cell was gradually increased. Readings of the voltage and current were made. At a certain point the voltage fall suddenly increased while the current simultaneously decreased. At the same time the surface of the anode brightened and bubbles of oxygen gas were evolved. This marks the change of the metal from the active to the passive state. The following curves in Fig. 1 show the results for 99.7% iron, 100% nickel, 98% cobalt, and 100% cobalt. Solutions of 0.2 *N* sulfuric acid, sodium sulfate, and potassium dichromate were used. The temperature was 0°. The following table gives the area of the respective anodes:

TABLE II.—AREA OF ANODES IN SQ. CM.

Metal	0.2 *N* H_2SO_4	0.2 *N* Na_2SO_4	0.2 *N* $K_2Cr_2O_7$
Iron (99.7%)	0.201	0.066	0.068
Nickel (100%)	0.120	0.068	0.068
Cobalt (98%)	0.087	0.085	0.168
Cobalt (100%)	0.15	0.045	0.045

From an inspection of these curves and by calculations it may be seen that nickel is passive in all the solutions and at all current densities.

Iron is passive at all current densities in potassium dichromate and sodium sulfate, and becomes passive at current densities above 6.0 amp. per sq. dcm. in 0.2 *N* sulfuric acid.

Cobalt becomes passive in 0.5 N sulfuric acid at 16–17 amp. per sq. dcm., in 0.2 N sodium sulfate at 24 amp. per sq. dcm. It is passive at all times in 0.2 N potassium dichromate.

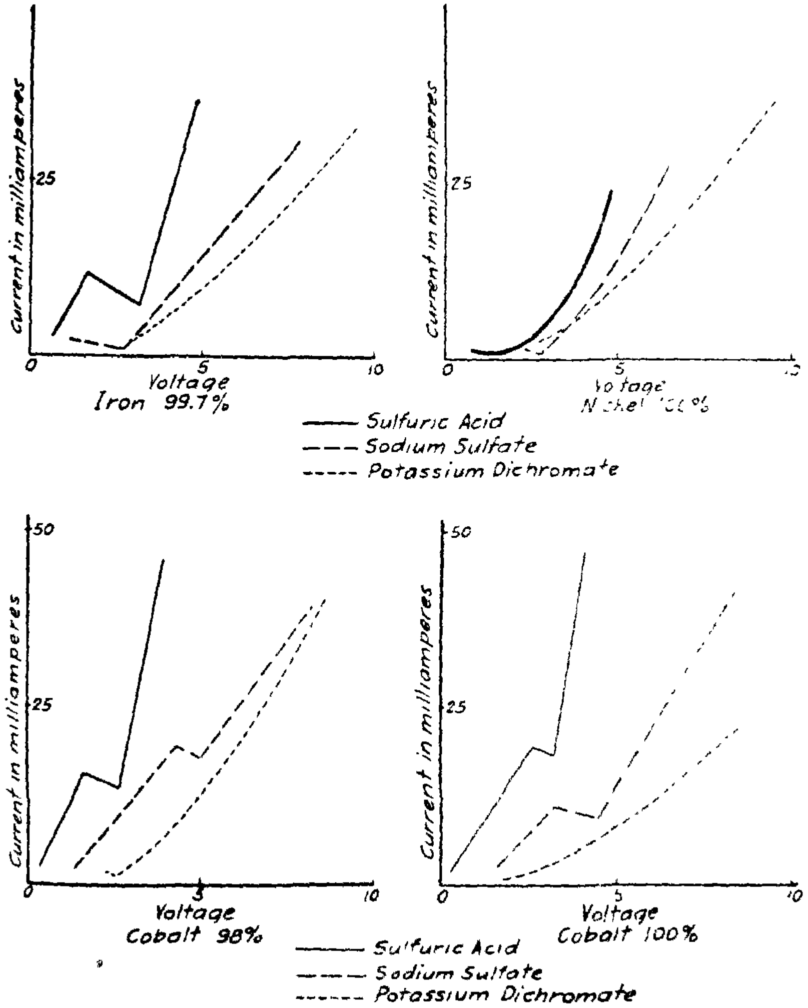

Fig. 1.

The above curves represent average experiments and values may be obtained which will differ slightly from those given. The time factor influences results. By this we mean that if the current density were somewhat lower than the above values, and the current were allowed to flow for a longer period of time, the metal would become passive. For ample, cobalt in 0.2 *N* sulfuric acid will become passive at a current density of 10 amp. per. sq. dcm. if the current is passed for a sufficient length of time.[1]

Summary.—Cobalt as an anode becomes passive if the current density is of a sufficiently high value. The passive state is indicated by an increased voltage drop, a decreased current, by the evolution of oxygen gas, and by the failure of the anode to go into solution.

III.

In this series of experiments, the potential of the anode was measured against that of a normal calomel electrode as zero. The potential was measured when no current was flowing and also when the anode was a part of a platinum-metal cell using various electrolytes. The potentiometer used was a Leeds and Northrup student potentiometer and measured voltage to the fourth decimal place. Owing to the nature of the work readings were made to the third place only. A Weston standard cell was used with the potentiometer. All measurements were made at 0°. The electrolyte was contained in a large test-tube. The anode was prepared by fastening the metal, either in the wire form or as a narrow strip, to a copper wire. This was sealed through a glass tube with sealing wax so that the metal only came in contact with the electrolyte. A platinum foil cathode was used. The calomel electrode was prepared in the usual manner and checked from time to time against amalgamated zinc in molar zinc sulfate, a voltage of 1.03 being obtained.

Metal	Active potential No current	Potential Current flowing	State of metal Current flowing
	A.—0.2 *N* Sulfuric Acid AT 0°.		
Iron (99.7%).......	—0.514	+1.911-1.887(10)[a]	Passive
Nickel (100%)......	—0.234	1.916-1.902(5)	Passive
Cobalt (98%)[b]......	—0.350	0.605-671(15)	Active
Cobalt (98%).	—0.278	1.888-1.849(15)	Passive
	B.—0.2 *N* Sodium Sulfate at 0°.		
Iron (99.7%).......	—0.616	1.959-1.971(5)[a]	Passive
Nickel (100%)......	—0.167	1.809-1.797(5)	Passive
Cobalt (98%)[b] ...	—0.411	0.270-0.250(5)	Active
Cobalt (98%).......	—0.411	1.811-1.824(5)	Passive
Cobalt (100%)[b]...	—0.416	0.302-0.264(5)	Active
Cobalt (100%)	—0.416	1.870-1.840(5)	Passive
	C.—0.2 *N* Potassium Dichromate at 0°.		
Iron (99.7%) .. .	—0.185	2.634-2.592(5)	Passive
Nickel (100%)......	—0.400	2.268-2.290(5)	Passive
Cobalt (100%)......	—0.306	2.422-2.522(5)	Passive

[a] Was not subjected to the initial high current to secure the passive state.

[b] The figures in parenthesis indicate the current in milliamperes flowing through the anode.

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[1] See THIS JOURNAL, 35, 767 (1913); 36, 2004 (1914).

The electrode was immersed in the electrolyte and its potential determined with no current flowing. Then a current of 50 milliamperes was allowed to flow through the anode until it became passive. The current was then reduced and the potential again measured. The current was allowed to flow for a long period of time and then the electrode was removed and the loss in weight checked against the copper equivalent from the copper coulometer. It seems to be impossible to get exact potential checks. This is due probably to variations in the electrode surface and in the current employed. It was found that fluctuations in the current very materially affected the potential The summary of the results obtained is shown in the preceding table.

The above results show (1) the metals in the active state possess a negative potential. Experiments show that this potential will vary with time[1] and with the material and surface of the cathode; (2) the potential of the anode when passive is positive and likewise varies with time. It was also found that the potential of the anode varied with the current flowing through it. For example, in 0.2 *N* potassium dichromate, the same passive cobalt anode will show a potential of 1 920 with a current of 5 milliamperes and a potential of 2.40 with a current of 10 milliamperes.

Summary.—A series of measurements of the anodic potentials of iron, nickel, and cobalt are given. From an inspection of the results it may be seen that when in the active condition and no current is flowing through the electrode, it has a negative potential. When the electrode is an anode with the current flowing, the potential changes in sign and increases in value even if the metal remains active. If, however, the metal becomes passive, the potential is markedly increased.

Conclusions.

The results of experiments show that, at low current densities, cobalt, when used as an anode, readily goes into solution. If the current densities are sufficiently high, the cobalt becomes passive and is insoluble. The voltage measurement of the cobalt-platinum cell, with various electrolytes and a comparison with similar results with iron and nickel, show that when the cobalt becomes passive there is a marked increase in the voltage across the cell. It may be seen from the potential measurements that this is due to the change in potential of the cobalt as it changes from the active to the positive state.

Cobalt may be classed with the passive metals since it exhibits all the characteristics of iron and nickel when they are passive. The essential difference between the cobalt and the other metals lies in the fact that the cobalt as an anode will not become passive at the low current densities required by nickel and iron. If cobalt assumes the passive state, it will remain so even though the current density is reduced. In the absence of the anodic relation, the cobalt becomes active in acid solution more readily than does nickel.

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[1] See also This Journal, 38, 363 (1916).

SEATTLE, WASHINGTON.

THE RAPID DETERMINATION OF CARBON MONOXIDE IN AIR.[1]

BY ARTHUR B. LAMB AND ALFRED T LARSON

Received June 28, 1919

The breathing of air containing 1% of carbon monoxide by men in moderate activity will lead to loss of consciousness within a few minutes, followed very soon by death. 0.1% of carbon monoxide may cause disablement in about 2 hours and 0 05% is sufficient to induce drowsiness on prolonged breathing.

The testing of the efficiency of gas mask absorbents for carbon monoxide, therefore, involves the precise analysis of air mixtures containing 1% and less of this gas. Moreover, to follow adequately the behavior of an absorbent during a test, frequent and very rapid analyses are required.

When testing of this nature became necessary in the Research Division of Chemical Warfare Service, a search for a satisfactory method was made, but none was found at once sufficiently accurate and rapid for this purpose.

Methods depending upon absorption, such as the cuprous chloride and the Haldane methods, were out of the question, since the volume changes to be measured at these concentrations were so minute. Conversion to carbon dioxide and its determination was not suitable because of the difficulty of securing rapid and at the same time complete absorption of carbon dioxide at very low concentrations. The liberation of iodine from iodine pentoxide furnished a very accurate method, particularly at concentrations of carbon monoxide as low as 0.1%, but it was found to be time consuming.

Thermometric methods depending on the rise of temperature produced by the combustion of the carbon monoxide had, to be sure, been described, particularly in the patent literature, and they had, at least, the merit of rapidity. Thus, Guasco[2] had proposed a differential air thermometer in which one of the bulbs was of platinum covered with platinum black. The device has been found to poison rapidly, requires frequent calibration, and is not accurate at low concentrations.

A. and L. D. Williams[3] had described an arrangement which employs

[1] Published by permission of Maj Gen W. L. Sibert, Director of Chemical Warfare Service, U. S. A.

[2] *Compt. rend.*, 155, 282 (1912).

[3] U. S. pat. 1,143,473. June, 1915

an electrically heated catalyst in contact with which the gas burns, the temperature rise being measured by a thermocouple. Unfortunately, the two thermojunctions are separately heated with the result that the accidental temperature differences at the two junctions introduce errors which may completely mask any heating effect resulting from the combustion of small quantities of carbon monoxide.

Phillip and Steele[1] had placed a catalytic material on a wire which was made one side of a Wheatstone bridge, the catalyst being heated by passing a current through the wire. No provision, however, was made to prevent poisoning of the active material; nor is the device sufficiently compensating to detect the small temperature changes resulting from carbon monoxide air mixtures of low concentration

B. C. Tilghman[2] and H. H. Clark[3] had suggested Wheatstone bridge arrangements in which one side of the bridge is heated to a temperature where combustion of the carbon monoxide takes place. These methods are, however, not truly differential and on that account are of little value for the quantitative measurement of low concentrations of carbon monoxide.

All of the above devices would no doubt be of value in the detection of relatively high concentrations of carbon monoxide, as, for instance, in the operation of signals, warning of the approach to the explosive limit. They would also be undoubtedly rapid in action, but their accuracy would be wholly insufficient for measurements of the low concentrations above mentioned.

Attempts were therefore made to increase the accuracy of the thermometric method without forfeiting its rapidity, and two new modifications of the method were developed which met this requirement. Both measure the temperature rise resulting from the combustion of carbon monoxide in air. In the first method, the combustion takes place in contact with a heated platinum wire, in which case the amount of combustion is constant but not complete. In the second method, combustion takes place in contact with a platinum catalyst and is complete. In the first method, the temperature rise is measured by a Wheatstone bridge arrangement, which is practically a platinum resistance thermometer; in the second the temperature rise is measured by a thermocouple.

Neither of these methods is an absolute one, that is, both must be calibrated by the use of carbon monoxide air mixtures of known concentrations. As a consequence the absolute accuracy of these methods depends, in part, upon how accurately these concentrations can be determined either by synthesis, or, as was found more convenient in practice, by analysis. Since these calibrations are but infrequently required and the analysis of the reference gas can be made at leisure, the method employed for the purpose need not be a rapid one and, therefore, a slow and very accurate method such as the one using iodine pentoxide can be employed. The absolute accuracy of these new methods can therefore be made equal to that of the best chemical method; since in addition they are rapid, they ought to prove useful in many fields.[1]

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[1] U. S pat. 899,068 Sept , 1908.

[2] U. S. pat. 524,361. Aug., 1894.

[3] U. S. pat. 960,823. June, 1910.

First Method (Hot Wire Method).[2]

In this method (Fig. 1) the air mixture to be analyzed is passed over a platinum wire heated to a dull red, in contact with which the combusti-

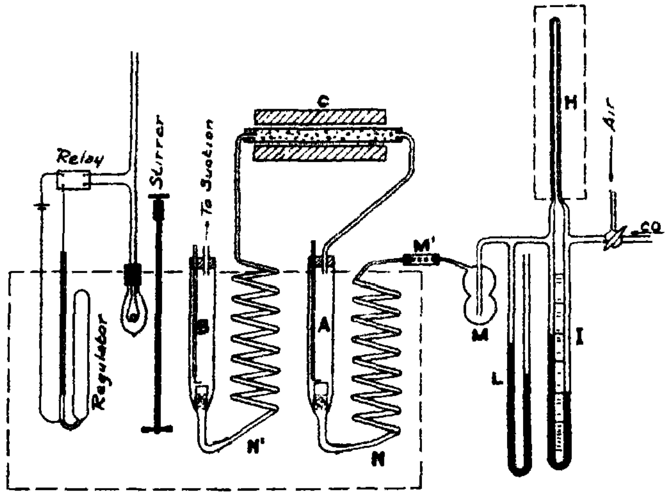

Fig. 1.

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[1] U. S. pats. 1,321,063 and 1,321,064 have been granted covering these two methods.

[2] This method finally proved less advantageous for our purposes than the second method (Catalytic Method) to be described later It was, therefore, not fully developed by us and can doubtless be brought to a much higher state of perfection Nevertheless, important details regarding it were worked out; it was put in actual operation, and tests made demonstrated its considerable reliability and accuracy. For this reason a brief description of it and its operation is given.

After our work on this method had been completed a valuable paper bearing on this subject was published by Weaver and Weibel of the Bureau of Standards (Bureau of Standards, *Scientific Paper* 334, "New Forms of Instruments for Showing the Presence and Amount of Combustible Gas in the Air"). In this paper important fundamental studies are given of the behavior of heated wires in air mixtures containing combustible gases. An apparatus is described for determining combustible gases working on a principle similar to the above-mentioned First Method. It is not, however, as rigorously differential as this method, in that instead of two identical wires, an active and a coated wire are employed. Moreover, it is not certain from the above paper that this apparatus, which evidently operated successfully as a detector at the concentrations studied, would at our 10 times lower concentrations operate with the precision required in our analytical work.

ble gas is partially burned, then through a tube of heated copper oxide where the combustion is completed. The gas mixture, free from carbon monoxide, then passes back over a second platinum wire not only in itself identical with the first wire, but identically mounted and connected in series with it. These two wires constitute two arms of a Wheatstone bridge and after being suitably balanced a change in temperature of either wire with respect to the other will cause a change in relative resistance, which is disclosed by a suitable galvanometer. This arrangement, except for the carbon dioxide formed and the slight change in volume, is rigorously differential. To insure identity of temperature in the surroundings and in the gas stream the whole apparatus is submerged in a closely regulated water thermostat, and the gas stream, before reaching the hot wires, is led through long, copper spirals similarly submerged.

The most serious difficulty and one which was underestimated at the outset, was the irregular variation in the relative resistance of the heated wires, even when no carbon monoxide was present in the gas stream. Thus, these relative resistances were found to vary markedly with changes in the total rate of flow of the gas in spite of apparent substantial identity in the dimensions and shapes of the hot wires and their containers. It was, therefore, necessary to hold the flow carefully constant by means of a sensitive flowmeter. In spite of these precautions large and irregular variations in the relative resistance of the two wires still occurred, so that the effect of the combustion of small concentrations of carbon monoxide on the first wire, was completely masked. The difficulty was finally solved by carefully eliminating eddies in the gas stream. This was accomplished by placing within "P" (Fig. 2) several layers of cotton gauze and covering the end of "P" with a fine-mesh cotton gauze over which the heated platinum wire was directly placed. This gave a steady and apparently stream-line flow and eliminated the marked fluctuations in the relative resistance of the wires.

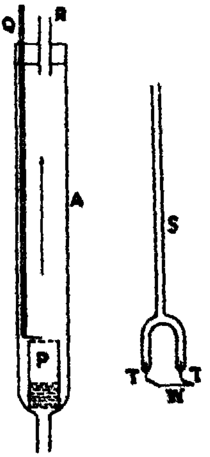

Fig. 2.

Apparatus.

The apparatus is shown assembled in Fig. 1. The platinum wires ("heaters") are supported within the tubes A and B. C is an electric furnace containing a tube of copper oxide. N and N′ are copper tubes wound in a spiral as indicated. H, I, is a flowmeter, the capillary of which is kept in the thermostat. L is a manometer which indicates changes in the pressure of air within the system. M is a wash-bottle for drying the gas while M′ is a glass-wool plug which serves to remove acid spray

An enlarged view of the heater and its containing tube is shown in Fig. 2. Into the glass fork S are sealed platinum wires (No. 14) which are bent sharply at right angles, the ends being one cm. apart. A slit was cut in the end of each wire and into this was clamped a strand of platinum wire, W, made by twisting together two wires 0.002 inch in diameter. Satisfactory contacts were made by arc welding the ends of the wire to the support. The fork was held rigidly so that the platinum heater fell

TABLE I.—DEFLECTION WITH 0.0976% MIXTURE OF CARBON MONOXIDE IN AIR.

Resistance D = 1100 ohms
Heating Current = 1.1 amperes
Rate of Flow = 1.5 liters per minute
1000 ohms additional resistance in galvanometer circuit.

E = 900 ohms and F = 77 ohms.
Galvanometer Resistance = 120 ohms.

Time	Galvanometer reading Cm	Total deflection Cm	Time of adjustment. Min
9.40 Air	−0.3		
9.58 Air	−0.3		
10:10 Air	−0.1		
10.17 Air	−0.2		
10:18 Gas Mixture	+24.0		
10:19 Gas Mixture	+22.2		
10:20 Gas Mixture	+22.0		
10:22 Gas Mixture	+21.7	21.4	9.5
10:23 Gas Mixture	+21.5		
10:27 Gas Mixture	+21.1		
10:29 Gas Mixture	+21.1		
10:32 Air	+0.7		
10:35 Air	−0.3		
10:42 Air	−0.3		
10:44 Air	−0.2		
10:46 Gas Mixture	+22.5	22.5	6.5
10.49 Gas Mixture	+22.5		
10:51 Gas Mixture	+22.3		
10:53 Gas Mixture	+22.3		
10:55 Air	−0.2		
10:57 Air	−0.3		
11:00 Air	−0.3		
11:03 Gas Mixture	+22.2	22.5	4.5
11:05 Gas Mixture	+22.1		
11:07 Gas Mixture	+22.1		
11:10 Air	−0.7		
11:12 Air	−0.7		
11:15 Air	−0.9		
11:17 Gas Mixture	+22.2	22.9	3.0
11:18 Gas Mixture	+22.1		
11:20 Air	−1.0		
11:23 Air	−1.0		
		22.4 ±0.4	5.7

just over the mouth of P. A storage battery large enough to maintain the wires at a constant, dull red for long periods was used. The current flowing through the bridge was kept constant by means of a slide-wire resistance and a millivoltmeter.

Results.

Results selected from a typical run with a 0.9976% mixture of carbon monoxide in air are given in Table I.

Similar results were obtained with mixtures containing 0.1% carbon monoxide. The percentage reproducibility in both cases was practically identical, being ±2% over an interval of one to two hours, and about 5 minutes was required to reach a definite deflection.

Second Method (Catalytic).

This method depends upon the catalytic combustion of the gas in contact with platinum. At 275–300° this reaction is fast enough so that combustion is complete under ordinary conditions. The temperature rise is measured by means of a thermocouple and galvanometer. After calibration, deflections of the galvanometer represent definite concentrations of carbon monoxide.

This method not only proved to be more accurate than the first method, but also easier to install and operate. It was used for many months in routine testing laboratories of the Chemical Warfare Service, and indeed, made possible the rapid development of carbon monoxide masks and absorbents.

Apparatus.

Two satisfactory types of apparatus were developed, one using a vapor and the other an air bath to heat the gas and the contact mass. The former apparatus is by far the easier to install and it alone will be described in detail in this paper.

A diagram of it is shown in Fig. 3; B was a steel tube 90 cm. long and 7.5 cm. in diameter, closed at one end. The tube was covered except for the upper 25 cm. with several thicknesses of asbestos paper. Boiling diphenylamine was found to give satisfactory results in the vapor bath though it decomposed slowly and had to be renewed from time to time. Sufficient heat to keep the zone of condensation within 30 cm. of the top of tube B was maintained.

The gas mixture to be analyzed was brought to the constant temperature of the vapor bath by a 4 mm. Pyrex glass tube extending to within 5 cm. of the bottom of the vapor jacket, whence it wound backward in a close coil about 15 cm. long and 6 cm. in diameter equivalent to a straight length of about 3 meters. Attached to this coil was the Pyrex glass tube A, 15 mm. in diameter and extending about 30 cm. above the top of the steel tube B. Tube D was fitted into A as indicated. This was made from a length of 4 mm. Pyrex glass tubing to which was attached a 20 cm. length of 7 mm. tubing, this enlarged portion being constructed as shown in the figure. This tube carried the catalyst and thermoelement shown in the enlarged cross-section given in Fig. 4. The thermocouple was made from No. 30 copper and constantan wires, the joints being welded or silver soldered. (If silver wire had been used instead of copper many of the difficulties resulting from the oxidation of the copper would probably have been avoided.) The distance between the two junctions was about 6 cm., this portion of the element being made of the constantan wire. The copper leads extended through the rubber connections and were attached to a galvanometer. A wall type d'Arsonval galvanometer, having a resistance of approximately 120 ohms and giving a deflection of about 0.30 cm. per microvolt on a curved scale 50 cm. from the galvanometer mirror, was used in this work.

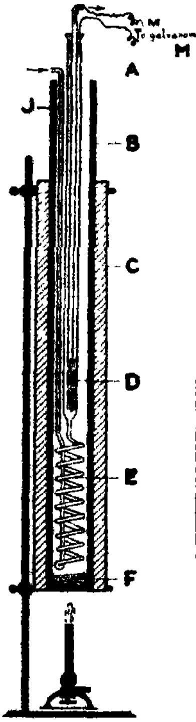

Fig. 3

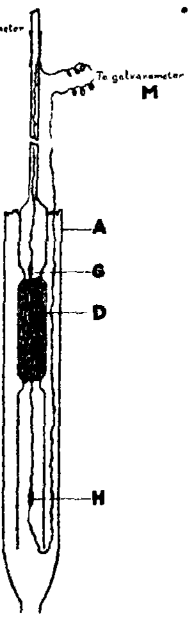

Fig 4.

Catalyst.

Catalysts were made, some from platinum wire, 0.05 mm. in diameter, and others from platinum gauze, woven from a similar wire When the wire was used, it was wound into the form of a 2 mm. spiral and then pressed into a fairly compact mass. One gram of this wire gave sufficient surface for our purpose. To prepare it the platinum was first cleaned with acid and then covered with platinum black by electroplating in a solution of chloroplatinic acid in the usual manner. When a heavy coating had been deposited, the wire was washed and then electrolyzed, first in dil. sodium hydroxide solution and then in dil. sulfuric acid, during which time the current was commutated as in the previous plating. This operation was found to be absolutely essential to the successful preparation of the catalyst. The catalyst was now washed and dried and placed in tube D, as shown in Fig. 4. Junction G lay near the upper surface of the catalyst and was as centrally located within the tube as possible. The catalyst was firmly packed into the tube so as to insure firm lodgment and to prevent channels through which the gas might pass without coming in contact with the catalyst.

This method could, of course, easily be made into a continuous recording one by the use of various electrical recording devices now in the market.

Calibration.

The apparatus was calibrated by passing through it air containing known percentages of carbon monoxide Because variable rates of flow produce variable galvanometer deflections, it was necessary to maintain a fixed rate of flow, which rate was governed by the nature of the testing to be done. The number of points to be determined for purposes of calibration was also governed largely by a similar consideration.[1]

To fix a given point, a certain concentration of gas was drawn through the machine until the galvanometer readings became constant. Two samples of the gas were then withdrawn and analyzed by the iodine pentoxide method. The concentration was now altered and a second point obtained, and so on, for as many points as seemed desirable. As an illustration, the results obtained in the calibration of an electrically heated apparatus (Unit No. 2, New Interior Building Laboratory) are given in Table II

TABLE II - CALIBRATION

CO in air mixture %	Galvanometer deflection		Deviation from empirical formula.	
	Observed Cm	Computed from empirical formula Cm	Cm	% total air.
0.057	4.5	4.75	−0.25	−0.003
0.104	8.8	8.70	+0.10	+0.001
0.264	22.8	22.73	+0.07	+0.001
0.441	39.0	39.16	−0.16	−0.002
0.706	(66.0)[a]	65.61	+0.39	+0.004
1.127	(111.8)[a]	112.09	−0.29	−0.003
			±0.21	±0.002

[a] In these measurements additional resistance had to be inserted in the galvanometer circuit

These results are represented graphically by the solid curve in Fig. 5. The observed deflections are represented by the empirical equation $D = 82(\%) + 15.5(\%)^2$ with an average deviation of only 2 mm.

It is of interest to compare the above observations with what would be expected had none of the heat of combustion been lost to the surroundings. In this computation the specific heat of air is taken as 0.237 at 275–300°, the molecular heat of combustion of carbon monoxide as 68040 calories, the temperature coefficient of e. m. f. as 57.03 microvolts per degree and the apparent molecular weight of air as 28.8. The galvanometer showed a deflection of 0.0323 cm. per microvolt of 1.84 cm. per degree. This would then require a deflection of 183.6 cm. for a 1% carbon monoxide air mixture, corresponding to a temperature rise of 99.66°. This value has been used to draw the dotted line in Fig. 5, representing the calculated deflections for different concentrations of carbon monoxide.

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[1] In the testing of absorbents for CO, a 1% CO air mixture has generally been used, although 0.5% and 0.25% have been found desirable at times. The "break" in the absorbent was usually taken as the point at which 0.1% CO leaked through These points on the galvanometer scale are therefore of considerable interest and it is important that CO air mixtures of about these concentrations be used in the calibration.

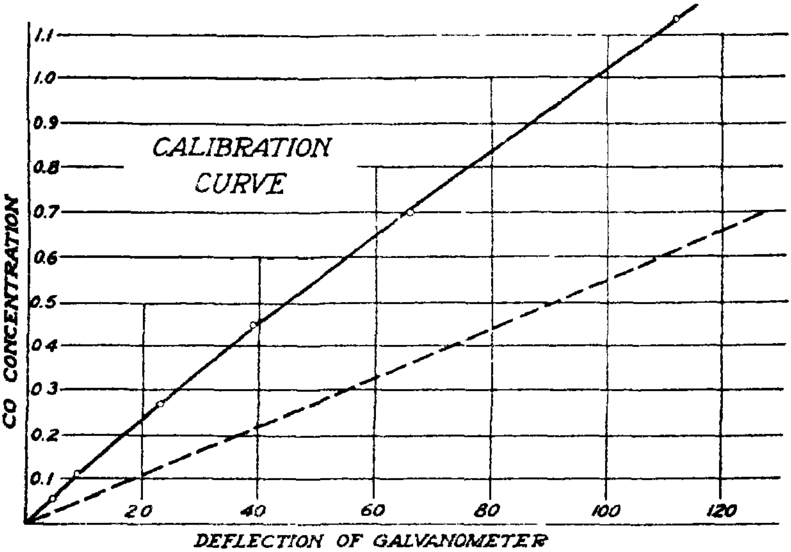

Fig. 5

The observed deflections for this apparatus are about half that calculated on this basis, showing that a very considerable dissipation of heat occurs. The gradual inflection of the curve representing the observed results indicating a lesser relative heat loss for higher concentrations and higher temperatures is interesting and is probably explained by the fact that at the higher temperatures a great increase in the reaction velocity occurs so that the reaction zone in the contact mass becomes smaller and hence the loss of heat by conduction less.

Longevity of Catalyst.

The successful operation of this device depends upon the permanence of the platinum catalyst. Anything which will change the character of the platinum black surface will impair and in some cases completely destroy its catalytic properties. A high temperature, for instance, will change the platinum black to a grey, which is considerably less active than the black. It was therefore important not only that there should be sufficient platinum to complete the combustion of the carbon monoxide present, but also that this surface should be in such excess that the heat generated per unit area of its surface was not great enough to effect the conversion to the grey variety.

The introduction of halogens into the gas stream produces permanent poisoning of the catalyst. When this occurs the catalyst must be removed from the apparatus and washed in hot nitric acid or even replated in some cases in order to bring it back to its former activity. Sulfur compounds were also injurious to the contact surface, but in such cases drawing pure air through the heated catalyst frequently restored it to its former effectiveness. The effect of sulfur dioxide on the catalyst is shown in the following table:

TABLE III.—EFFECT OF SULFUR DIOXIDE ON CATALYST

Concentration of CO, approx. 0.2%. Temperature of air bath, 300°. Unit No. Ia.

Time.	Gal. deflection Cm.
5.20	25.3
SO_2 introduced 1 part per 100,000 (by volume)	
5.23	24.6
5.26	23.3
5.30	23.1
5.35	22.6
5.40	21.9
5.45	21.2
5.50	20.5
5.55	19.8
6.00	19.1
6.05	18.4
6.10	17.7
6.15	17.0
6.16 SO_2 off	
6.17	19.0
6.19	19.6
6.30	19.6

It will be noted that the rate of "fatigue" is proportional to the time, being 0.7 cm. for each 5-minute interval. When the sulfur dioxide was turned off, the galvanometer deflection increased and finally reached a constant value, though one lower than at the outset. If the temperature be raised to 350° and air passed at the same time, this poisoning effect can be entirely removed.

A few of the most frequent sources of halogens and sulfur compounds which were encountered and which must be guarded against deserve mention. When carbon dioxide is made by the dehydration of formic acid, the conc. sulfuric acid used suffers slight decomposition into sulfur dioxide. Again, when the gas is dried by *bubbling* through conc. sulfuric acid enough acid spray is carried along with the gas to give trouble. Rubber connections made from fresh, cold-cured rubber give off sulfur chloride and must be heated in strong alkali before use. The air with which the carbon monoxide is being diluted often causes trouble. It was found advisable to draw the air from out of doors, in order to eliminate every possibility of contamination. Some absorbents give off gases which produce poisoning effect, in which case provision has to be made for their removal.

When precautions were taken to avoid these rather patent sources of contamination no difficulties were experienced. The same catalyst mass was often employed almost continuously for many weeks without replacement. It is advisable, however, when a machine is in constant use, to check its reading against a reference gas once a day, or better still, before and after prolonged series of tests. Any slight poisoning of the catalyst would then be disclosed and correction for it could be made.

Accuracy of Catalytic Method.

An estimate of the accuracy of this method can be gained from the close agreement of the observed galvanometer deflections obtained with

Table IV.—Reproducibility of Deflection with 0.1% CO Air Mixture.

Concentration of CO = 0.117% (by volume).
Rate of flow = 1.47 liters per minute.
Temperature of bath = 275°.

Time Min.		Galv. deflection Cm.	
0	air	0.3	12.3*
1	0.1% CO	10.5	
3		12.1	
5		12.3	
6		12.4	
7		12.5	
8		12.6	
10	air	0.7	
14		0.5	12.3
16		0.3	
19		0.3	
21	0.1% CO	12.3	
22		12.4	
24		12.6	
25		12.6	
26		12.6	
30	air	0.4	12.3
33		0.3	
35	0.1% CO	12.0	
36		12.5	
37		12.6	
38		12.6	
41	air	0.5	
44		0.3	

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* When these values are referred to the calibration curve (Fig. 4) it will be noted that the galvanometer deflections are greater than one would expect for gas of this concentration. The pure carbon monoxide used in this test had been kept in a galvanized tank for sometime and the high reading is no doubt due to the added heat of combustion of the hydrogen which had accumulated in the tank.

different concentrations of carbon monoxide in calibrating an apparatus, for instance No 11*a*, with the empirical formula $D = 85(\%) + 15.5(\%)^2$, characteristic of it. As can be seen from Table III, the average percentage deviation here from the formula was ±0.002%, over the whole range, based on the air.

The reproducibility of the readings is shown by the following table (Table IV) where observations made when air and a 0.1% carbon monoxide mixture were alternately drawn through the machine are recorded.

It is evident that over this interval the galvanometer readings are reproducible to within a millimeter or to within 1%: this corresponds to an absolute reproducibility in this mixture of 0.001% carbon monoxide based on the total air.

The reliability of this device in the estimation of carbon monoxide is further shown by the results tabulated below. This table (Table V)

TABLE V—COMPARATIVE EFFICIENCIES

Carbon Monoxide Canister. A—Thermometric Method B—Iodine Pentoxide Method Against 1% CO Air Mixture

	Canister No 20						
Mins	5	45	120	165	195	235.	248.
% Leakage by A	0.2	0.3	0.5	1.0	1.5	4.8	10.0
% Leakage by B	0.5	1.0	1.1	1.2	2.1	4.7	11.7
% B − % A	0.3	—0.7	0.6	0.1	0.6	—0.1	—1.7
	Canister No 21.						
Mins	5	45	120	165	200	230.	254.
% Leakage by A	0.2	0.1	0.3	0.5	2.4	5.1	9.7
% Leakage by B	0.3	0.0	0.6	0.6	2.5	5.0	10.5
% B − % A	—0.1	0.1	—0.3	—0.1	—0.1	0.1	—0.8
	Canister No 22.						
Mins	5	45.	120	156	170.	180.	
% Leakage by A	0.3	1.1	1.7	5.3	9.8	15.7	...
% Leakage by B	0.8	1.4	1.8	5.7	10.7	16.1	...
% B − % A	—0.5	—0.3	—0.1	—0.4	—0.9	—0.3	..
	Canister No 23						
Mins	5	45	120	165.	176.	183	
% Leakage by A	0.1	0.4	0.8	5.0	10.3	15.3	...
% Leakage by B	0.0	0.0	0.5	4.6	8.9	15.5	...
% B − % A	0.1	0.4	0.2	0.4	1.4	—0.2	...
	Canister No 24						
Mins.	5	45	120.	165.	184	200.	215.
% Leakage by A	0.0	0.1	0.2	1.4	4.9	9.8	15.0
% Leakage by B	0.0	0.0	0.0	1.1	4.8	10.5	15.3
% B − % A	0.0	0.1	0.2	0.3	0.1	—0.7	—0.3
	Canister No 25						
Mins.	45	120	150	190	211.		
% Leakage by A	0.4	1.2	5.0	9.6	14.7	...	..
% Leakage by B	0.8	1.1	4.6	10.3	14.5	..	...
% B — % A	—0.4	0.1	0.4	—0.7	0.2	...	...

contains the results of a series of carbon monoxide canister tests in which the iodine pentoxide method and this thermometric method were both used in testing the effluent gases. At every point where an analysis was made by the chemical method a similar analysis was made by the thermometric device. The fine agreement of the two methods shows the new one to be entirely trustworthy.

Assuming for the moment that the values obtained by the iodine pentoxide method are correct, the average discrepancy of the above results by the thermometric method is only 0.38%. At first glance this might appear to be a large average where such small quantities (0.2%–10.0%) are concerned, but when it is remembered that the tests are made on a 1% gas and that, therefore, this percentage variation corresponds only to an error of 0.0038% on the total air mixture, it will be recognized that this represents a very excellent agreement. This agreement is especially satisfactory when it is remembered that the results were secured in routine runs made under the stress of war-time demands.

Actually, since the thermometric method was calibrated by means of iodine pentoxide, the above discrepancies are essentially accidental, and should not all be charged to the thermometric method. In other words, the real discrepancies are presumably somewhat less than 0.0038%.

Summarizing our observations regarding the accuracy of this catalytic method (Method No. 2), we would say that at least on mixtures of 0.1 to 1% of carbon monoxide the method can reasonably be relied upon for an accuracy of ±0.003%, based on the total air.

Summary.

1. The necessity for an accurate and rapid method for the analysis of dilute carbon monoxide air mixtures in the study of gas mask absorbents for carbon monoxide has been explained.

2. Two thermometric methods answering this requirement have been described. In the first method the gas mixture is passed over a platinum wire heated to redness and the carbon monoxide is partially burned in contact with it. The gas mixture is then freed of carbon monoxide by passing through heated copper oxide and is brought back in a thermostat over another identical platinum wire heated by the same electric current. The first wire is the hotter because of the combustion which occurs on it—and the resultant relative change in the resistance of the two wires serves as a measure of the concentration of the carbon monoxide. In the second method the mixture is passed through a platinized, platinum catalyst when the carbon monoxide is completely burnt. The temperature rise is measured by a thermoelement and indicates the concentrations of the carbon monoxide.

3. Both methods are rapid. The latter is particularly accurate, easy to install and to operate. With reasonable precautions the activity of

its catalyst remains constant so that machines have been in constant satisfactory operation for many weeks at a time. Being very nearly instantaneous these methods are particularly useful for continuous analysis of a changing gas mixture. Attempts to apply them to the analysis of flue and combustion gases are already under way.

WASHINGTON, D. C.

[CONTRIBUTION FROM THE KENT CHEMICAL LABORATORY OF THE UNIVERSITY OF CHICAGO.]

STUDIES IN CONDUCTIVITY. VI. THE BEHAVIOR OF MIXTURES OF TWO SALTS CONTAINING A COMMON ION IN ANHYDROUS FORMIC ACID SOLUTION.

BY H. I. SCHLESINGER AND F. H. REED [1]

Received July 28, 1919.

The first 4 papers of this series[2] have dealt with the agreement of solutions of formates in anhydrous formic acid with the demands of the law of mass action, when the degree of ionization is determined by the conductivity method, although in such solutions these electrolytes are very highly ionized. Since highly ionized substances in other solvents do not obey this law, there exist at present no measurements for strong electrolytes which can be used to verify the deductions which are made from the law for the behavior of mixtures of two electrolytes with a common ion. An investigation of such mixtures therefore seemed desirable, especially as agreement with the law in the behavior of the mixtures, as well as of the individual salts, would dispose of the possibility that the agreement in the case of the latter is due to any accidental cancellation of deviations.[3] This study, in addition to having fulfilled the purposes just mentioned, has resulted in bringing out some points that may lead to a better understanding of concentrated solutions and has thrown further light on the peculiar behavior of the formates of the alkaline earths.

In most details the methods of Schlesinger and Martin were followed without change except for the following points: The formic acid was prepared by distilling Baker & Adamson's acid, prepared especially for our work, from $^1/_{10}$ its volume of phosphorus pentoxide at 20° to 27°, and a pressure of 10 to 18 mm. Three distillations, in the apparatus already described, usually produced an acid with a specific conductivity of about 6.5 × 10^{-6} reciprocal ohms. The formates were made as by Schlesinger and Coleman; they were recrystallized from absolute alcohol until their conductivities in solution were unchanged by further recrystallization. The formates of strontium and calcium used were parts of the samples prepared by Schlesinger and Mullinix. All salts were analyzed by conversion into sulfates and were found pure within the limits of the analytical method. All solutions were made by weighing the salt directly into the 25 cc. volumetric flasks. Weights were corrected to vacuum. The conductivities were measured by the Washburn modification of the Wheatstone-Kohlrausch method with the special precautions, the necessity for which was pointed out in the fifth paper of this series.[1]

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[1] The work reported in this and the preceding paper of this series has been presented to the Faculty of the Ogden Graduate School of Science of the University of Chicago by F. H. Reed in partial fulfillment of the requirements for the degree of Doctor of Philosophy. The work was completed in June, 1917.

[2] Schlesinger and collaborators as follows: With Calvert, THIS JOURNAL, 33, 1924 (1911); with Martin, *Ibid.*, 36, 1589 (1914); with Coleman, *Ibid.*, 38, 271 (1916), with Mullinix, *Ibid.*, 41, 72 (1919).

[3] See also the seventh paper of the series [illegible]

Ionization Constants.

For the interpretation of our work on the mixed solutions an accurate knowledge of the ionization constants of the salts investigated is necessary. When these constants were taken from the earlier work of this series, for which an accuracy of from 0.2 to 0.3% was quite sufficient, it was found that the calculated results showed certain irregularities which we ascribed to very slight errors in the relative values of the various ionization constants employed. Since our improved apparatus and methods, described in the paper referred to above, enabled us to determine the conductivities of solutions with a maximum average error of slightly less than 0.05%, it was deemed advisable to redetermine these constants. Tables I, II and III show the results obtained. In each case no more determinations were made than were needed to cover a sufficient range of concentration to make dependable the average value of the ionization constant of that salt. In the first column of each of these tables is given the concentration of each of the respective salts expressed in gram mols

TABLE I.—THE CONDUCTIVITY OF POTASSIUM FORMATE SOLUTION AT 25° IN ANHYDROUS FORMIC ACID

Conc	X.	X_a	λa	α	K	% error
0			68.92			
0.1027	0.006581	0.006516	63.43	0.920	1.092	0.01
0.1314	0.008232	0.008167	62.18	0.902	1.092	0.02
0.1804	0.01093	0.01086	60.22	0.874	1.091	0.01
0.1992	0.01193	0.01187	59.55	0.864	1.095	0.06
0.2312	0.01356	0.01350	58.39	0.847	1.086	0.05
0.2433	0.01418	0.01411	57.99	0.841	1.087	0.04
0.2696	0.01549	0.01543	57.24	0.831	1.097	0.09
0.2792	0.01595	0.01589	56.90	0.826	1.091	0.02
0.3104	0.01744	0.01738	55.99	0.812	1.092	0.03
0.3232	0.01802	0.01796	55.58	0.806	1.085	0.06
0.3253	0.01813	0.01806	55.52	0.806	1.086	0.06
0.3266	0.01818	0.01812	55.48	0.805	1.085	0.07
					Av., 1.090	

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[1] Schlesinger and Reed, THIS JOURNAL, 41, 1727 (1919).

TABLE II.—THE CONDUCTIVITY OF SODIUM FORMATE SOLUTION AT 25° IN ANHYDROUS FORMIC ACID

Conc	X	X_a	λ_a	α	K	% error
0			66.225			
0.06418	0.004025	0.003960	61.70	0.932	0.815	0.04
0.06881	0.004289	0.004225	61.39	0.927	0.810	0.00
0.08375	0.005135	0.005071	60.54	0.914	0.816	0.06
0.09682	0.005850	0.005786	59.75	0.902	0.807	0.04
0.1755	0.009888	0.009820	55.94	0.845	0.806	0.06
0.2068	0.01137	0.01131	54.67	0.826	0.808	0.03
0.2337	0.01262	0.01256	53.72	0.811	0.814	0.04
0.2528	0.01346	0.01340	53.00	0.800	0.810	0.01
0.2734	0.01436	0.01429	52.28	0.789	0.809	0.02
0.2954	0.01529	0.01522	51.54	0.778	0.807	0.07
0.3153	0.01613	0.01606	50.94	0.769	0.808	0.05
				Av.	0.810	

per liter of solution; in Col. 2 the specific conductivity (X) at 25° ± 0.01°, in reciprocal ohms; in Col. 3 the specific conductivity (X_a) corrected for the conductivity of the solvent; in Col. 4 the equivalent conductivity (λ_a) calculated from the corrected specific conductivity; in Col. 5 the degree of ionization (α) the necessary λ_0 being found as described in the earlier papers of this series; in Col. 6 the ionization constant (K) as calculated from the equation $\alpha^2C/(1-\alpha) = K$; in Col. 7 the percentage error in the measured specific conductivity which would account for the deviation of the individual values of K from

TABLE III.—THE CONDUCTIVITY OF LITHIUM FORMATE SOLUTION AT 25° IN ANHYDROUS FORMIC ACID

Conc	X	X_a	λ_a	α	K	% error.
0			64.72			
0.06709	0.003978	0.003917	58.38	0.902	0.557	0.01
0.09025	0.005180	0.005116	56.68	0.876	0.557	0.00
0.1018	0.005752	0.005689	55.86	0.863	0.554	0.06
0.1248	0.006861	0.006797	54.46	0.841	0.557	0.01
0.1438	0.007737	0.007673	53.37	0.825	0.557	0.01
0.1524	0.008122	0.008061	52.90	0.817	0.557	0.01
0.1658	0.008722	0.008658	52.21	0.807	0.558	0.02
0.1749	0.009116	0.009053	51.77	0.800	0.559	0.06
0.1750	0.009114	0.009053	51.73	0.799	0.557	0.00
0.1915	0.009811	0.009750	50.92	0.787	0.556	0.03
0.1916	0.009835	0.009773	50.95	0.787	0.559	0.06
0.2044	0.01036	0.01030	50.38	0.778	0.559	0.06
0.2196	0.01099	0.01092	49.73	0.768	0.559	0.07
0.2480	0.01209	0.01203	48.51	0.750	0.556	0.03
0.2596	0.01253	0.01247	48.01	0.742	[0.553]	0.16
0.3076	0.01429	0.01423	46.24	0.714	[0.550]	0.30
				Av.,*	0.557	

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* The bracketed values were not used in obtaining the average because they were obtained from solutions so concentrated that the mass law is no longer observed

the average value. This percentage error is given because relatively large deviations in the constant may be due to very small errors in the conductivity, which is the measured quantity showing the net experimental error. It will be seen that in every case this error is less than 0.1%, and is in nearly all cases very much less.

Method of Calculation.

By the use of the constants thus determined a method for the calculation of the specific conductivity of a solution of a mixture of any two of these salts (*e. g.*, sodium and potassium formates) was developed as follows: The specific conductivity (X_m) of such a mixture is considered the sum of the specific conductivity (X_1) of the first salt (sodium formate), and of the specific conductivity (X_2) of the second salt (potassium formate); or, $X_m = X_1 + X_2$. Now, in general, if λ represents the equivalent conductivity, X the specific conductivity, α the degree of ionization, and C the concentration, the relation holds that $1000\ X/C = \lambda = \alpha\lambda_o$, where λ_o is the equivalent conductivity at infinite dilution; or it may be written in the form

$$1000\ X = \alpha\lambda_o C.$$

Consequently,

$$1000\ X_m \doteq \alpha_1\lambda'_o C_1 + \alpha_2\lambda''_o C_2, \qquad (1)$$

in the right hand member of which equation the first term gives the specific conductivity of one of the salts, and the second term that of the other salt.[1] It may be noted that the only unknown terms in this equation are the respective degrees of ionization of the two salts. If it is assumed for the present that one of these, α_2, is known (the method of finding it will be discussed later), it is possible to find an expression for α_1 in terms of α_2 and other known quantities as follows:

Upon the basis of the assumption that the law of chemical equilibrium is obeyed when these two salts containing a common ion are present together in a solution, the ionization constants K_1 and K_2 may be expressed thus, respectively:

$$\alpha_1(\alpha_1 C_1 + \alpha_2 C_2)/(1 - \alpha_1) = K_1, \qquad (2)$$

$$\alpha_2(\alpha_1 C_1 + \alpha_2 C_2)/(1 - \alpha_2) = K_2, \qquad (3)$$

from which, dividing (2) by (3), we obtain:

$$\alpha_1 = \frac{\alpha_2 K_1/K_2}{1 - \alpha_2(1 - K_1/K_2)} \qquad (4)$$

Since K_1 and K_2 are known for the salts in question, Equation 4 makes the calculation of α_1 very simple when α_2 is known.

Equation 3 may be written

$$\alpha_1 C_1 + \alpha_2 C_2 = K_2(1 - \alpha_2)/\alpha_2.$$

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[1] Terms with subscript 1 refer in general to one of the salts; terms with subscript 2 to the other

Dividing by α_2 we obtain

$$C_2 + C_1\alpha_1/\alpha_2 = K_2(1 - \alpha_2)/\alpha_2^2. \qquad (5)$$

The law of mass action reads

$$\alpha_2^2C/(1 - \alpha_2) = K_2, \text{ or } C = K_2(1 - \alpha_2)/\alpha_2^2. \qquad (6)$$

Now it is self evident that C in Equation 6 represents a concentration of the second salt in a solution containing that salt only, in which the degree of ionization, α_2, is the same as it is in the mixture of the two salts for which Equation 5 holds. Calling this concentration C_s, we may rewrite Equation 5

$$C_2 + C_1\alpha_1/\alpha_2 = C_s \qquad (7)$$

In order to use the equations just given, we now calculate for a series of arbitrarily chosen values of α_2 the corresponding values of α_1 and C_s by use of Equations 4 and 6, and plot α_1/α_2 against either C_s or α_2.[1] The first step in the calculation is to chose a value for C_s which might be the one in which the ionization of the second salt in a solution of that salt only is the same as it is in the mixture for which the calculation is to be made. In order to test the correctness of this value, we read off from the plot the value of α_1/α_2, corresponding to that of C_s which has been chosen, and from the known values of C_1 and C_2 calculate the numerical value of the expression $C_2 + C_1\alpha_1/\alpha_2$. If this is equal to C_s, as demanded by Equation 7, the value chosen for C_s is correct; if it is not, we must choose another value for C_s and continue by a method of trial until the correct value is obtained.

This method of calculation may be illustrated in the case of Expt. 14, Table V. The sum of the concentrations of the two salts is about 0.219. Since this is not all potassium formate it is clear that a solution of this salt alone in which the concentration is somewhat less than 0.219 would be ionized to the same extent as the potassium formate in the mixture.[2] We therefore assume for C_s the value 0.21; from the curve, the corresponding value of α_1/α_2 is 0.9532. Now C_2 and C_1 in this experiment were, respectively, 0.05699 and 0.1622, whence $C_2 + C_1\alpha_1/\alpha_2 = 0.2116$, a value of C_s different from that assumed. Since α_1/α_2 decreases as C_s increases, it is evident that a higher value of C_s must be assumed; finally assuming the value 0.2115 for C_s, the corresponding α_1/α_2 is 0.953 and $C_2 + C_1\alpha_1/\alpha_2 = 0.21156$, which is sufficiently close to 0.2115 to be considered identical. From the second plot and the value 0.953 for α_1/α_2, we now find that α_2 is 0.857,[3] whence α_1 is 0.8167. We can now use these values in testing the experimental data. If both salts in the mixture obey the mass law and if the equivalent conductances of none of the ions is affected by the other ions or molecules present, the specific conductivity of the mixture should, according to Equation 1, be 0.01214, whereas experiment gave 0.01215.

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[1] Other combinations could be used for these plots, but the two mentioned are the most convenient.

[2] Note that for C_s we always use the data for the salt of greater ionization which is the second salt of the mixtures.

[3] From the value 0.2115 for C_s and Equation 6 the value of α_2 might be calculated but the use of the second curve is simpler.

This method of calculation[1] has proved quite simple and accurate. All curves were plotted to such scale that the conductivities of the mixed solutions could be calculated with an accuracy as great as that of the measurements.

When $C_1 = C_2$, as is true of a number of the experiments, the calculation can be somewhat simplified, as in this case Equation 2 becomes

$$C = K_1(1 - \alpha_1)/\alpha_1(\alpha_1 + \alpha_2). \tag{8}$$

Table IV contains the data used in constructing the curves for the calculation of the conductivity of mixed solutions. It will be understood from the foregoing discussion that these data are derived from the ionization constants given in the preceding section of this paper and from those given by Schlesinger and Mullinix[2] in the case of the alkaline earth formates and therefore are in no way dependent on the values found for the conductivities of the mixed solutions. The first column contains the values for α_2, which are arbitrarily chosen at uniform intervals and which in the mixture of potassium formate with sodium, with lithium and with strontium formate, refer to the degree of ionization of the potassium salt. For the mixtures of strontium formate with calcium formate, α_2 refers to the degree of ionization of strontium formate. The next 5 columns show the corresponding degree of ionization of the other salts, as calculated by Equation 4. In order to make clear to what mixture each set of data refers, the symbols $\alpha_{1,\mathrm{Na}}$, $\alpha_{1,\mathrm{Li}}$, $\alpha_{1,\mathrm{Sr}}$, $\alpha_{1,\mathrm{Ca}}$ have been used. It will be noted that two sets of values of $\alpha_{1,\mathrm{Sr}}$, the degree of ionization of strontium formate, corresponding to the values for potassium formate given in the first column, are to be found in Cols. 4 and 5; the significance of this will be explained later. Attention may be called to the fact that values of α_1 and of C_s, corresponding to those of α_2, have not been given in all cases—only those values required for the calculations have been included in the table. Col. 7 gives the value C_K, which is identical with C_s of Equation 7 when potassium formate is the second salt of the mixture and Col. 8, the value of C_{Sr}, which is the same as C_s when the second salt of the mixture is strontium formate.[3]

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[1] Calculations of this sort have been made in aqueous solutions by the isohydric principle. When the mass law is supposed to be obeyed, the isohydric principle in the simple form is applicable only to those cases in which the ionization constants are very small—a point which is sometimes overlooked.

[2] *Loc. cit.*

[3] In the mixtures of strontium and potassium formate the latter is considered the second salt.

TABLE IV.—DATA FOR THE CALCULATION OF THE CONDUCTIVITIES OF SOLUTIONS AND MIXTURES[a]

α_i	$\alpha_{i,\mathrm{Na}}$	$\alpha_{i,\mathrm{Li}}$	$\alpha'_{i,\mathrm{Sr}}$	$\alpha''_{i,\mathrm{Sr}}$	$\alpha_{i,\mathrm{Ca}}$	C_K	C_{Sr}
0.670					0.6255		0.3767
0.680					0.6361		0.3554
0.690					0.6468		0.3344
0.700					0.6575		0.3144
0.710					0.6682		0.2955
0.720					0.6790		0.2774
0.730					0.6898		0.2602
0.740					0.7007		0.2439
0.750		0.6052			0.7116	0.4845	0.2283
0.760		0.6180			0.7226	0.4529	0.2134
0.770		0.6311			0.7336	0.4227	0.1992
0.780		0.6443			0.7448	0.3942	0.1857
0.790	0.7365	0.6578		0.6393	0.7558	0.3667	0.1728
0.800	0.7483	0.6715		0.6534	0.7669	0.3406	0.1605
0.810	0.7601	0.6854		0.6677	0.7781	0.3156	0.1487
0.820	0.7720	0.6995		0.6822	0.7894	0.2918	0.1375
0.830	0.7839	0.7139	0.5340	0.6970	0.8006	0.2690	0.1267
0.840	0.7960	0.7285	0.5530	0.7121		0.2472	
0.850	0.8081	0.7433	0.5718	0.7275		0.2263	
0.860	0.8203	0.7584	0.5914	0.7432		0.2063	
0.870	0.8326	0.7737	0.6119	0.7593		0.1872	
0.880	0.8449	0.7893	0.6334	0.7755		0.1680	
0.890	0.8574		0.6559	0.7922		0.1514	
0.900	0.8699		0.6795	0.8092		0.1346	
0.910	0.8826		0.7043	0.8265		0.1184	
0.920	0.8953		0.7304			0.1030	
0.930			0.7578			0.0882	

[a] The ionization constants used in the calculation of the data in this table are 1.00, 0.810, 0.557, 0.514 and 0.422 for potassium, sodium, lithium, strontium and calcium formates respectively. The first 3 values are taken from the first section of this paper, the others from the work of Schlesinger and Mullinix (*loc. cit.*). The values given in that paper are slightly different from those used here. This is due to the fact that the work herein reported was completed before that of Mullinix and consequently we used his preliminary values for the constants and the conductivity at zero concentration of the two alkaline earth formates. A recalculation of a few of the data with the final values has shown that no change of importance is introduced into the results or conclusions and as the calculations require a great deal of time they have not been repeated.

Solutions Containing a Mixture of Two Uni-univalent Salts.

Table V gives the results of the work done with solutions of mixtures of sodium and potassium formates. The first column of the table gives the number of the experiment since this information is required for later reference, and Col. 9 shows the percentage deviation between the specific conductivities Col. 7, calculated on the assumption that the mass law holds in the solutions of the mixtures for both salts by the method just discussed, and the experimentally determined specific ductivities Col. 8. The meanings of the headings of the other columns have already been given.

TABLE V.—THE CONDUCTIVITY OF SOLUTIONS OF MIXTURES OF SODIUM AND POTASSIUM FORMATES IN ANHYDROUS FORMIC ACID AT 25°.

Expt.	C_3.	C_1	C_2	α_1	α_2	X calc	X found	% error.
8	.	0 05288	0 05288	0 894	0 919	0 006481	0 006492	0 17
9	.	0 05306	0 05306	0 894	0 919	0 006500	0 006512	0 19
10	. .	0 06197	0 06197	0 880	0 908	0 007488	0 007486	0 02
4	.	0 07113	0 07114	0 866	0 897	0 008475	0 008478	0 03
2	. .	0 08755	0 08755	0 843	0 879	0 01019	0 010195	0 06
5	.	0 1014	0 1014	0 825	0 864	0 01158	0 01159	0.10
11	0 2025	0 1081	0 09941	0 823	0 862	0 01179	0 01178	0 13
14	0 2115	0 1622	0 05699	0 817	0 857	0 01214	0 01215	0 03
7	..	0 1076	0 1076	0 818	0 858	0 01219	0 01219	0 02
12	0 2188	0 08522	0 1377	0 812	0 853	0 01268	0 01269	0 06
13	0 2381	0 1493	0 09645	0 801	0 844	0 01353	0 01351	0 22
3	. .	0 1231	0 1231	0 800	0 843	0 01367	0 01369	0 12
6	..	0 1304	0 1304	0 792	0 837	0 01436	0 01440	0 24
16	0 2645	0 1344	0 1375	0 786	0 832	0 01489	0 01491	0 15
1	. ..	0 1476	0 1476	0 775	0 822	0 01593	0 01592	0 06
15	.	0 1628	0 1628	0 761	0 810	0 01729	0 01728	0 05
17	.	0 1807	0 1867	0 739	0 792	0 01933	0 01929	0 22

Similar measurements and calculations made for solutions of mixtures of lithium and potassium formates are presented in Table VI. It is of interest to note that the mixtures of sodium and potassium formates represent a case in which the ionization constants of the two salts (0.810 and 1.09, respectively) do not differ very greatly, while for the mixtures of lithium and potassium formates the difference in the constants (0 557 and 1.09, respectively) is much greater.

TABLE VI.—THE CONDUCTIVITY OF SOLUTIONS OF MIXTURES OF LITHIUM AND POTASSIUM FORMATES IN ANHYDROUS FORMIC ACID AT 25°.

Expt.	C_3.	C_1	C_2.	α_1.	α_2	X calc	X found	% error.
2	. ..	0 08933	0 08932	0 789	0 880	0 009976	0 009981	0 02
6	0 1821	0 1216	0 07373	0 778	0 873	0 01056	0 01056	0 01
7	. .	0 1082	0 1082	0 761	0 862	0 01175	0 01174	0 04
3	....	0 1159	0 1159	0 750	0 854	0 01244	0 01244	0 02
8	.. .	0 1219	0 1219	0 742	0 849	0 01298	0 01299	0 06
4	0 2401	0 2231	0 04618	0 733	0 843	0 01327	0 01326	0 05
5	0.2348	0 07511	0 1694	0 737	0 846	0 01346	0 01346	0 00
1	.. .	0 1374	0 1374	0 722	0 836	0 01434	0 01434	0 02
9	0.2801	0 1618	0 1415	0 707	0 825	0 01545	0 01544	0 05
13	0 2631	0 2241	0 06986	0 718	0 833	0 01442	0 01439	0.31
11	0 2860	0 2266	0 09227	0 703	0 822	0 01554	0 01549	0.32
14	0.3124	0 2002	0 1428	0 687	0 811	0 01689	0 01681	0.46
12	0.3271	0 2233	0 1388	0 679	0 805	0 01752	0 01741	0.62

It will be seen from Table V that the experimentally determined conductivity of solutions containing both sodium and potassium formates agrees extremely well with the value calculated on the assumption that the mass law is applicable in these mixtures The maximum deviation is 0 24%, which can easily be accounted for by errors less than 0 1% in the conductivity measurements on which the values of the ionization constants of the two salts were based The mixtures of lithium and potassium formates show an even better agreement as inspection of the first 9 lines of Table VI shows, the maximum deviation being only 0 06%. This result may be taken as fairly definite proof that the agreement between the demands of the mass law and the actual behavior of the uni-univalent formates in anhydrous formic acid solutions is a real and not merely an apparent one

The last 4 measurements shown in Table VI require further discussion. It has been shown in an earlier paper[1] of this series that the agreement between the mass law and the behavior of the alkali formate solutions ceases when fairly high concentrations are reached as is of course to be expected It was thought that the behavior of the concentrated mixed solutions might throw some light on the question of concentrated solutions in general, and a few measurements were therefore made While this part of the work has merely been begun, the results are of sufficient interest for a brief discussion It was pointed out in the earlier papers that the point at which these formates begin to deviate from the mass law is not the same for any of the salts investigated While it is of course impossible to determine exactly what that point is, it may be stated that, for example, the lithium formate solutions begin to deviate from the law at a concentration in the neighborhood of 0 25 N with potassium formate, on the other hand, deviation commences only above 0 40 N It seemed therefore that some information might be obtained by determining approximately the concentration at which a mixture of these two salts would begin to show a similar deviation For this purpose the last 4 measurements found in Table VI were made and for a discussion of the results Table VII, containing measurements taken from Tables III and VI and calculations based upon them, was constructed Col 1 of Table VII gives the number of the measurement from III or VI, the symbol Li indicating that lithium salt alone is present, the symbol Li K that the measurement is for a mixture Col 2 gives the total concentration of salt dissolved, Col 3 that of the undissociated lithium formate; Col 4 that of the lithium ions, Col 5 that of the undissociated potassium formate, Col 6 that of the potassium ion, Col 7 that of the formate ion, Col 8 the total concentration of undissociated molecules, Col 9 the total concentration of ions, Col 10 the concentration of all molecular species, *i e*, ions and undissociated molecules, and Col 11 gives the percentage deviation of the specific conductivity of each solution from the demands of the mass law.

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[1] Schlesinger and Martin, *Loc cit*

TABLE VII.

Expt.	Total conc.	Conc. HCOOLi undis.	Conc Li^+ ion.	Conc. HCOOK undis.	Conc. K^+ ion.	Conc HCOO⁻ ion.	Total conc. mols.	Total conc. ions.	Conc mols + ions.	% dev.
5 Li-K..	0.2445	0.0197	0.0554	0.0261	0.1433	0.1987	0.0458	0.3974	0.4432	0.00
32 Li....	0.2480	0.0620	0.1860			0.1860	0.0620	0.3720	0.4340	−0.03
33 Li....	0.2596	0.0670	0.1926			0.1926	0.0670	0.3852	0.4522	−0.16
4 Li-K..	0.2693	0.0596	0.1635	0.0073	0.0389	0.2024	0.0669	0.4048	0.4717	−0.05
13 Li-K.	0.2940	0.0632	0.1609	0.0117	0.0582	0.2191	0.0749	0.4382	0.5831	−0.31
9 Li-K..	0.3033	0.0474	0.1144	0.0248	0.1167	0.2311	0.0722	0.4622	0.5344	−0.05
14 Li..	0.3076	0.0880	0.2196			0.2196	0.0880	0.4392	0.5272	−0.30
11 Li-K..	0.3189	0.0673	0.1593	0.0165	0.0758	0.2351	0.0838	0.4702	0.5540	−0.32
14 Li-K....	0.3430	0.0627	0.1375	0.0270	0.1158	0.2533	0.0897	0.5066	0.5963	−0.46
12 Li-K..	0.3621	0.0717	0.1516	0.0271	0.1117	0.2633	0.0988	0.5266	0.6254	−0.62

It will be seen from the table that the total concentration of dissolved substance is not the factor which determines when deviation begins. Nor is it the total amount of either salt, for when lithium formate is alone present the concentration of the first solution which shows decided deviation is 0.2596; in the mixtures, however, a solution containing only 0.224 moles (*i. e.*, 0.0632 moles of undissociated and 0.1609 moles of dissociated lithium salt) of lithium formate is already deviating. On the other hand, a solution containing in a mixture almost the same amount of this salt, namely 0.223 moles per liter (*i. e.*, 0.0596 moles of undissociated and 0.1635 moles of dissociated lithium salt) does not deviate. If now the various data given in Table VII are examined in this way it will be seen that of all the various factors included, only the concentration of the undissociated lithium formate shows any parallelism with the deviations of the concentrated solutions. Thus, it seems that no matter whether there is potassium formate present or not, no matter what the total number of molecules or of ions, no matter what the number of the 3 kinds of ions present, deviation from the mass law occurs when the wider concentration of the undissociated lithium formate is above 0.062.[1] We may therefore tentatively conclude that in the more concentrated solutions the deviation is essentially due to a deviation from the mass law in the behavior of the undissociated molecules, or at least due to some factor which is proportional to the concentration of the undissociated molecules.[2]

Solutions Containing Either One Uni-univalent and One Uni-bivalent or Two Uni-bivalent Formates.

In an earlier paper of this series,[3] the peculiar behavior of the formates of the alkaline earth metals was pointed out. These salts, although they are uni-bivalent, appear to be judged by the conductivities of their solutions, to obey the mass law as derived for uni-univalent salts within a range of concentration from about 0.1 to 0.35 equivalent. Above the upper limit named they behave in the manner characteristic of the behavior of the alkali metal formates;[1] below the lower limit, however, there is a deviation which corresponds to a greater ionization than is to be expected from the law obeyed in the middle range of concentration. It was pointed out that the behavior of these salts might be taken to indicate that they ionize in moderate concentrations into two ions only—*i. e.*, into formate and an alkali metal formate ion—and that only in quite dilute solutions does ionization into the simple ions take place. There were, however, reasons for doubting the correctness of this conclusion, and it was therefore also suggested that the apparent agreement with the law for uni-univalent salts in the moderate concentrations might be due to a cancellation of two deviations in opposite directions—namely the deviation noted in concentrated and that noted in dilute solutions. In order to gain further light on this question the behavior of mixtures containing these salts was studied.

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[1] Any deviation less than 0.1% is considered due to experimental error

[2] It should be noted that in the concentrated solutions the conductivity, and therefore the degree of ionization, are smaller than demanded by the mass laws.

[3] Schlesinger and Mullinix, *Loc. cit.*

In calculating the conductivities which would be exhibited by mixtures, for example, of potassium and strontium formates from the constants given in this paper and the preceding one of this series a number of points must be borne in mind. Let us assume, first, that both salts ionize into two ions only. In this case the ionization constant for the strontium salt given by Schlesinger and Mullinix[2] cannot be directly used in the equations developed above for the calculation of the value of the conductivities of the mixed solutions from the ionization constants, since in calculating the constant for strontium formate the concentrations were expressed in gram equivalents per liter. For use in the mass law the concentrations should be in moles. By following out the line of reasoning employed in deriving the equations for the mixtures containing only uni-univalent salts in the case now under consideration, it can be shown that the same equations can be used, if instead of using the constant given by Schlesinger and Mullinix we divide this constant by two and express the concentrations of the strontium salt in terms of gram equivalents. It is possible, however, to make another assumption with regard to the mode of ionization of the strontium salt, namely, that it breaks up into strontium ion and two formate ions but that it nevertheless follows the equation of the mass law which is applicable when there are only two ions formed. The calculation of the conductivities of the mixtures of potassium and strontium formates on this assumption can be shown to be exactly like the calculations made for the mixtures containing only alkali metal formates, provided the ionization constant for the strontium salt as given by Schlesinger and Mullinix is used and the concentrations are again expressed in gram equivalents per liter. In order to make the calculations on each of these assumptions, two sets of values for α_1 had to be calculated and two plots had to be made. The values calculated for the first assumption are called $\alpha'_{1,\mathrm{Sr}}$ in Table IV and those for the second assumption, $\alpha''_{1\,\mathrm{Sr}}$. The comparison of the calculated value for the conductivity of the mixtures with the value found by experiment is made in Tables VIII*a* and VIII*b*. Table VIII*a* contains the data for the calculation on the basis of the first assumption and VIII*b* those for the calculation on the second assumption. Inspection of the tables shows that neither of the calculated values agrees at all with the conductivities found. In order to make sure that this result is not due to an error in the value of the constant for the strontium formate or to some other cause peculiar to the strontium salt, the conductivites of a few mixtures of potassium formate and calcium formate were measured, but as the results were exactly similar to those with the strontium salts they have not been included. In Table IX data and calculations for mixtures of calcium and strontium formates are given. It can be shown that the method of calculation to be used for this case is the same as that used for mixtures of uni-univalent salts on either of the

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[1] See the second paper of the series, *Loc. cit.*

[2] *Loc. cit.*

TABLE VIII.—THE CONDUCTIVITY OF SOLUTIONS OF MIXTURES OF STRONTIUM AND POTASSIUM FORMATES IN ANHYDROUS FORMIC ACID AT 25°

TABLE VIII*a*

C_s	C_1	C_2	α_1	α_2	X calc.[a]	X found	% dev.
0.09193	0.06565	0.06536	0.751	0.927	0.006973	0.007043	1.0
0.1042	0.07530	0.07433	0.728	0.919	0.007818	0.007939	1.5
0.1172	0.1224	0.06969	0.706	0.911	0.009278	0.009413	1.5
0.1225	0.09025	0.08777	0.698	0.908	0.009062	0.009140	0.9
0.1339	0.2526	0.03843	0.681	0.900	0.01213	0.01229	1.3
0.1554	0.06337	0.1322	0.651	0.888	0.01042	0.01057	1.5
0.1555	0.1580	0.09763	0.650	0.888	0.01180	0.01200	1.7
0.1604	0.1162	0.1181	0.644	0.885	0.01145	0.01166	1.8
0.2348	0.1947	0.1699	0.564	0.846	0.01613	0.01652	2.4

TABLE VIII*b*

C_s	C_1	C_2	α_1	α_2	X calc.[a]	X found	% dev.
0.1248	0.06565	0.06536	0.820	0.906	0.007134	0.007043	1.3
0.1417	0.07530	0.07433	0.802	0.896	0.008013	0.007939	0.9
0.1674	0.09025	0.08777	0.777	0.881	0.009305	0.009140	1.8
0.1771	0.1224	0.06969	0.768	0.875	0.009538	0.009413	1.3
0.1875	0.06337	0.1322	0.759	0.870	0.01065	0.01057	0.7
0.2179	0.1162	0.1181	0.734	0.854	0.01178	0.01166	1.1
0.2325	0.1580	0.09763	0.723	0.847	0.01217	0.01200	1.4
0.2521	0.2526	0.03843	0.709	0.838	0.01234	0.01229	0.6
0.3296	0.1947	0.1699	0.661	0.805	0.01673	0.01652	1.3

[a] The values of the equivalent conductivity and infinite dilution used in obtaining these values of X_{calc} are 68.02 and 56.72 for the potassium and the strontium formate, respectively.

two assumptions made above and that the concentrations may for either case be expressed in equivalents, as was done in the original paper of Schlesinger and Mullinix, and that the values of the constants given by them are to be employed. The "second" salt of the mixture, that of higher degree of ionization, is in this case strontium formate and the subscript 1 therefore refers to the calcium and the subscript 2 to the strontium salt. The calculated values again fail to agree with the experimental ones. It is clear that neither of the assumptions made above represents correctly the behavior of these salts. It is likely, therefore, that both modes of ionization occur—*i. e.*, into intermediate ions and into the simple ions, but this point is not yet considered established.[1]

TABLE IX.—THE CONDUCTIVITY OF SOLUTIONS OF MIXTURES OF CALCIUM AND STRONTIUM FORMATES IN ANHYDROUS FORMIC ACID AT 25°.

No	C_s	C_1	C_2	α_1	α_2	X calc.[a]	X found.	% dev
10	0.1343	0.06482	0.07183	0.793	0.823	0.006177	0.006139	0.61
8	0.1727	0.08953	0.08701	0.756	0.790	0.007618	0.007569	0.64
9	0.1905	0.09815	0.09685	0.741	0.776	0.008261	0.008224	0.44
3	0.2143	0.1254	0.09512	0.722	0.759	0.009071	0.009042	0.32
7	0.2258	0.1176	0.1141	0.713	0.752	0.009470	0.009433	0.39
2	0.2802	0.1494	0.1394	0.677	0.718	0.01124	0.01119	0.49
6	0.2821	0.1485	0.1421	0.676	0.717	0.01130	0.01125	0.42
1	0.2892	0.1792	0.1204	0.672	0.713	0.01149	0.01144	0.44
5		0.1617	0.1617	0.658	0.700	0.01227	0.01222	0.41
4	0.3299	0.1834	0.1579	0.649	0.692	0.01274	0.01269	0.42
11	0.3441	0.1812	0.1745	0.642	0.685	0.01317	0.01308	0.71
12	0.3714	0.1950	0.1893	0.628	0.673	0.01395	0.01386	0.64

[a] The value used for the equivalent conductivity of calcium formate at infinite dilution is 54.94. For strontium formate that given for Table IX was used.

Summary.

1. A method of calculating from the ionization constants the degree of ionization of each of two salts containing a common ion, when the two salts are both present in solution, has been developed for the case in which both salts obey the mass law.

2. It has been found that in solutions of mixtures of sodium and potassium formates, as well as of lithium and potassium formates, the mass law is obeyed by both of the highly ionized salts present. On the other hand, solutions of mixtures containing as one, or as both of the salts, alkaline earth formates do not conform to the law, although these uni-bivalent salts when in solution alone seem to follow the law over a certain range of concentration. *This seems to make it quite certain that whenever the agreement of the salt with the law is merely an accidental one, solutions of mixtures containing such a salt will not obey this law. Hence we may conclude quite definitely that the agreement between the behavior of the*

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[1] Further evidence is presented in the seventh paper of this series, which follows.

alkaline metal formates, in anhydrous formic acid solutions, and the demands of the mass law is a real, and not an accidental one.

3. As is to be expected, when the total concentration of mixed solutions becomes relatively great, deviation from the mass law occurs also in the solutions which contain only uni-univalent formates. It has been found that this deviation seems to begin when the concentration of the undissociated molecules of one of the salts reaches the same value as that at which deviation begins in the solution of that salt by itself. This seems to be independent of the concentration of the other molecular species present and to indicate that in the concentrated solutions it is the undissociated molecules and not the ions which cause deviation from the mass law or at least that the undissociated molecules cause deviation at lower concentrations than do the ions.[1]

CHICAGO, ILL.

[CONTRIBUTION FROM THE KENT CHEMICAL LABORATORY OF THE UNIVERSITY OF CHICAGO.]

STUDIES IN CONDUCTIVITY. VII. TRANSFERENCE NUMBERS OF THE FORMATES OF SODIUM, POTASSIUM AND CALCIUM IN ANHYDROUS FORMIC ACID.

BY H. I. SCHLESINGER AND E. N. BUNTING.[2]

Received July 28, 1919.

The work of the preceding papers of this series,[3] particulary that of the sixth one, has proved that the agreement in the behavior of the formates of the alkali metals, when dissolved in formic acid, with the demands of the mass law is a real and not an accidental one so far as it is possible to establish this conclusion by the use of conductivity data alone. The only weakness in the argument lies in the fact that from the conductivity data two constants must be calculated for each salt—the ionization constant and the conductivity at infinite dilution, the latter of which must be obtained by extrapolation. If, however, we assume that the conductivity at infinite dilution obtained in this way for one of the salts is correct, we can calculate from this value and the transference numbers of this and the other salts the conductivity at infinite dilution for those salts without the use of conductivity data or extrapolation. By carrying out measurements of transference numbers we have in the work reported in this paper finally confirmed the conclusion mentioned above.[1] We have included also measurements of the transference number of calcium formate in order to gain further information concerning the alkaline earth formates which, as has been shown in the fourth paper of the series, display an anomolous behavior. In addition to establishing the points mentioned above, this work has resulted in data which it is hoped will be of aid in shedding light on the problem of the solvation of ions.

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[1] It must be recalled that the deviation herein referred to is of a different type from that commonly known in moderately dilute aqueous solutions of strong electrolytes (see the second paper of the series) in which the undissociated molecules are likewise frequently believed to be the deviating species.

[2] The work herein reported has been presented to the Faculty of the Ogden Graduate School of Science of the University of Chicago by E. N. Bunting in partial fulfillment of the requirements for the degree of Doctor of Philosophy. The work was completed in the summer of 1918.

[3] Schlesinger and collaborators, THIS JOURNAL, 33, 1924 (1911); 36, 1589 (1914); 38, 271 (1916), 41, 72, 1727, 1921 (1919).

The analysis of formic acid solutions of the alkali metal formates by the usual methods with the degree of accuracy required for even fairly reliable measurements of transport numbers, presents difficulties which it seemed unlikely that we would overcome readily. It was therefore decided that the most convenient and most accurate method would be found in measurement of the conductivity of the solutions before and after the electrolysis. Before carrying this plan into effect it was necessary, however, to make sure that no products are formed at the electrodes during electrolysis which might influence the conductivity. Solutions of the 3 salts for which transport numbers were to be determined were therefore separately electrolyzed between platinum electrodes, the quantity of current used was measured by a silver coulometer and the gaseous products were analyzed. The hydrogen given off at the cathode was found to correspond to a 100% yield according to the electrolytic equation

$$2Na^+ + 2\ominus + 2HCOOH \longrightarrow 2HCOONa + H_2.$$

At the anode the amount of carbon dioxide given off was found to correspond to 97% of that calculated on the basis of the equation

$$2COOH^- + 2\oplus \longrightarrow CO_2 + HCOOH.$$

Carbon dioxide is extremely soluble in formic acid and, while the electrolysis was run for a considerable length of time before beginning the measurements in order to saturate the solution, it is possible that some carbon dioxide was lost on this account. It is more likely, however, that some carbon monoxide and some oxygen may have been formed at the anode by secondary reactions as has been reported by Hopfgartner.[2] It is therefore clear that at the cathode no new ions or other products which might affect the conductivity are formed. At the anode the production of carbon monoxide is in all likelihood accompanied by the formation of water according to the equation

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[1] It was our intention to compare the transference numbers obtained by the Hittorf method with those obtained from concentration cells, but the latter part of this program was interrupted by duties arising out of the war.

[2] *Monatsh.*, 32, 523 (1911). No data on the current yields are given in this paper. This work, however, made it unnecessary to investigate the products further.

$$2COOH^- + 2\oplus \longrightarrow CO + CO_2 + H_2O.$$

The amount of water formed in this way is apparently too small to affect the results except perhaps in the most concentrated solutions. It was also feared that the great solubility of the carbon dioxide in the solutions might result in a change of the conductivity but experiments showed that neither the conductivity of the pure acid nor that of the salt solutions was appreciably affected by saturating with the dry gas. The conductivity method of analysis was several times checked by gravimetric analysis of the solutions after electrolysis and the two methods gave the same results within the limit of analytical error.

The transport cell employed,[1] of the usual W type with an inlet for filling at the top of the middle bend, had a capacity of about 200 cc., the column of liquid was about 70 cm. in length; the electrodes were of platinum foil about 3 sq. cm. in area, and the current used was 0.03–0.05 amperes. It could be run from 4 to 5 hours without appreciably changing the middle portion. The ordinary form of coulometer, consisting of a platinum dish, 15% silver nitrate solution and a silver disk anode wrapped in filter paper, was used; this form has been shown to be accurate within 0.05%.

The method of making a transference run was as follows: The apparatus containing about 200 cc. of a solution of known concentration was immersed in a thermostat at 25.00° ± 0.01° and the current was passed through the solution for 4 to 5 hours, depending on the concentration. The conductivity of the solution was measured before any of it was subjected to electrolysis and also at the end of the run. For this latter purpose 15 cc. was removed from the mid-portion through the opening in the apparatus provided for this purpose. In general the conductivity of the mid-portion remained unchanged or changed by less than 0.1%; runs in which the difference was greater were rejected and are not included in the tables given below. At the close of the run, 50 cc. was withdrawn from both the cathode and the anode portion by means of a pipet and transferred to two glass stoppered bottles in which the contents of each could be thoroughly mixed by shaking. After this the conductivity of each solution was measured. As a result of the withdrawal of solution from the ends of the columns, the latter had of course separated in the middle and had become divided into two parts, which may be called the sub-anode and the sub-cathode portions; these portions were run into bottles, and weighed, and their conductivities measured after each was thoroughly shaken.[1] After the removal of these various portions of solution from the cell, the latter was weighed in order to determine how much of the solution remained. This quantity of solution, usually from 0.3 to 0.4 cc., was assumed to be equally divided between anode and cathode portion and was added to the two portions in this way in the calculations. It was shown by experiment and by calculation that the amount of liquid lost during electrolysis by volatilization and spraying of the solution at the electrodes was small enough to be negligible.

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[1] The first cell made had electrodes of platinum deposited on the glass at various points within the cell in order that the conductivity of the solutions might be measured at various distances from the electrodes without removing the solution from the cell. While these electrodes were very small, local electrolysis nevertheless occurred and the resulting evolution of gas stirred up the solution. On this account and because the method of pipetting out a portion of the liquid proved satisfactory the scheme was abandoned. We now believe, however, that this plan can be carried out and that it would lead to accurate results, if successful.

As has been pointed out, the conductivity was used to determined the concentrations of the various portions of the solution after electrolysis. For this purpose equations based on the data of Schlesinger and Reed[2] and of Schlesinger and Mullinix[3] were used. For the sodium formate solutions the equation is:

$$1/\lambda = 0.01510 + 0.2815\chi,^4$$

for the potassium formate

$$1/\lambda = 0.01451 + 0.1936\chi,$$

and for calcium formate,

$$1/\lambda = 0.018185 + 0.7818\chi,$$

where λ is the equivalent conductivity, χ_1 the specific conductivity in reciprocal ohms corrected for the conductivity of the solvent. The first constant is $1/\lambda_0$, *i. e.*, the reciprocal of the conductivity at infinite dilution as determined by the method described in the earlier papers of this series; and the second constant is equal to the fraction $1000/K\lambda^2_0$, in which K is the ionization constant. From the value of λ obtained by the use of these equations and our experimental data the concentration in equivalents was directly calculated. The specific conductivities were measured in the cells and by the methods described in the fifth paper of this series. The densities of the solutions which were needed for the calculations could be found from the concentrations by means of equations of the type:

$$D = A + BC,$$

in which A and B are constants, D is the density of the solutions and C the concentration. The values for B for sodium, potassium and calcium formate solutions, respectively, are 0.036, 0.041 and 0.038 at 25° and the constant A is the density of the pure acid, 1.2142. The values of these constants were determined by a series of density determinations and reproduce the densities of the solutions within 0.05%, which is ample for the present purpose.

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[1] In a number of experiments no liquid was withdrawn by pipet from the anode and cathode portions, but the whole of each was collected in bottles, as were the portions described as sub-anode and sub-cathode portions above.

[2] THIS JOURNAL, 33, 6445 (1911).

[3] See the fourth paper of this series, *Loc. cit.*

[4] Equations of this type represent a form of the Ostwald dilution law. See the second paper of this series.

In order to avoid the necessity of tabulating all of the data required for the calculations and thus making the tables unduly long, the method of calculating the transference numbers will be illustrated in the following:

In one of the runs on potassium formate the conductivity of the original solution, corrected for the conductivity of the solvent was 0.011871 reciprocal ohm, the conductivity of the mid-portion at the close of the run was the same. The conductivities of the cathode and sub-cathode portions were, respectively, 0.013614 and 0.012642, whence the concentrations of the original solution of the cathode and of the sub-cathode portions are calculated to be, respectively, 0.19953, 0.23343 and 0.21439, the corresponding densities are 1.22238, 1.22377 and 1.22299. The volume of the cathode portion was 50 cc., from the concentration and density just given we find that it contained 60.207 g. of formic acid and 0.011672 gram equivalents of potassium formate. The weight of the sub-cathode portion was 31.370 g. From the concentration and density of this portion we find that it contained 30.907 g. of the acid and 0.005499 gram equivalents of the salt. The total weight of the solvent in the cathode portion was therefore 91.114 g. and the total weight of the salt was 0.017171 gram equivalents. As a result of electrolysis, however, some of the acid in the cathode portion is decomposed. In the run under discussion 0.007832 Faraday was passed through the solution. From the equation $2K^+ + 2HCOOH + 2\ominus = 2HCOOK + H_2$ we calculated the amount of acid decomposed to be $0.007832 \times 46.01 = 0.360$ gram. The original weight of the solvent in the cathode portion was therefore 91.475 g. From the concentration and the density of the original solution we find that this weight of solvent had contained 0.015140 gram equivalents of the salt before electrolysis. The amount of potassium transferred was then 0.017171 — 0.015140 or 0.002031 equivalents. This number divided by the number of Faradays which caused the transference is the transference number of the potassium ion. The number of Faradays is equal to the number of equivalents of silver, *G*, deposited in the coulometer if a correction for the current carried by the solvent is made. This is done by multiplying the quantity *G* by a fraction obtained by dividing the conductivity of the solution corrected in the usual way for the conductivity of the solvent by the uncorrected conductivity of the solution. The transference number can of course also be calculated from the loss of potassium at the anode. The calculation is like that described except for one point. At the anode, as a result of the reaction $2COOH^- + 2\oplus = HCOOH + CO_2$, $^1/_2$ equivalent of formic acid is produced per Faraday of electricity. The amount of acid calculated from this equation must therefore be subtracted from the weight of the solvent contained in the anode portion at the close of the run. Since the reaction at the anode does not proceed quite quantitatively according to the equation given, as has been shown above, the results at the cathode may be more reliable, but the data on sodium formate show that in moderately concentrated solutions the effect is negligible. Each of the determinations was subjected to 3 tests to check its reliability: first, the closeness of agreement between the results obtained at the anode and those at the cathode; second, the constancy of the conductivity of the mid-portion; third, the sum of the amounts of salt contained in all of the portions analyzed at the close of electrolysis had to be within 0.1% of the total amount of salt originally put into the apparatus. Runs which did not satisfy these requirements are, with but one or two exceptions, not included in the tables.

Tables I, II and III, which contain the data for the experiments on the transference numbers of sodium, potassium and calcium formates, respectively, are arranged as follows: Under C is the original concentration in gram equivalents per liter; under W, the weight in g. of the solvent in the cathode and in the anode portions, respectively, corrected as described above; under M, the gram equivalents of salt contained in W g. of the solvent in the cathode and in the anode portions; under E, the number of equivalents of positive ion constituent transferred to the cathode and from the anode, respectively; under N, the number of equivalents of electricity passed through the solution, corrected for the conductivity of the solvent; under T, the transference number of the positive ion calculated from the change at the cathode and from that at the anode; under T_{av}, the average of the values given under T for each experiment; under T_c, the average of all of the transference numbers obtained for any one concentration. It will be noted that the data for the anode portion are given in the row just below that on which the corresponding concentration is placed and that the data for the cathode are placed on the row above. The data under T_c have been obtained by weighing the results at each concentration in proportion as they appear to meet the requirements mentioned in the preceding paragraph. T_c has been omitted in the case of sodium formate because for this salt all of the data refer to practically the same concentration.

Table I.—Transference Data for NaOCHO in (Anhydrous) Formic Acid.

C.		W.	M.	E.	N.	T	T_{av}
	cathode	129.395	0.028212	0.001462		0.221	
0.2494					0.006601		0.220
	anode	135.224	0.026525	0.001430		0.219	
	cathode	128.549	0.028211	0.001593		0.220	
0.2498					0.007232		0.220
	anode	129.651	0.025266	0.001590		0.220	
	cathode	122.883	0.027217	0.001741		0.220	
0.2501					0.007909		0.220
	anode	131.019	0.025426	0.001737		0.220	
	cathode	119.443	0.026803	0.001698		0.226	
0.2536					0.007522		0.220
	anode	123.087	0.024266	0.001615		0.215	
						Mean	0.220

The data show that the method employed is capable of yielding accurate results under favorable conditions since the transference numbers for sodium formate show excellent agreement, not only for the different experiments but also when the results at the anode are compared with those at the cathode, most of them being practically identical with each other. It is clear, therefore, that the formation of a small amount of water at the anode can have but very little effect in moderate concentra-

TABLE II.—TRANSFERENCE DATA FOR KOCHO IN (ANHYDROUS) FORMIC ACID.

C.		*W.*	*M.*	*E.*	*N.*	*T.*	$T_{av.}$	T_c.
	cathode	108.973	0.0099749	0 0009975		0 269		
0.09982					0 003660		0.268	
	anode	105 577	0 0077313	0 0009787		0 267		
	cathode	104 109	0 0095835	0 0009955		0 275		
0.09981					0 003622		0 270	
	anode	108 794	0.0080161	0 0009584		0 265		
								0 269
	cathode	91 475	0 017171	0 002031		0 259		
0 1995					0 007832		0 259	
	anode	116 600	0 017274	0 002024		0 258		
	cathode	103 203	0 019060	0 001880		0 260		
0 2007					0 007230		0 256	
	anode	104 810	0 015632	0 001815		0 251		
								0 258
	cathode	105 328	0 028163	0 001729		0 247		
0.3015					0 006992		. .	
	anode	105 825	0 024753	0 001806		0 258		
	cathode	110 224	0 030078	0 002202		0 251		
0 3038					0 008770		0 249	
	anode	114 857	0 026877	0 002170		0 247		
	cathode	108 667	0 030790	0 002295		0 248		
0.3149					0 009264		0 249	
	anode	113 194	0 027374	0 002309		0 249		
								0.249
0 3906[*]	anode	103 886	0 034063	0 002797	0 01166	0 240		
	cathode	107 958	0 038163	0 002719		0 241		
0 3930					0 01127		0 244	
	anode	107 825	0 032290	0 002784		0 247		
								0 244

[*] An error was made in the cathode portion of this run

TABLE III.—TRANSFERENCE DATA FOR $Ca(OCHO)_2$ IN (ANHYDROUS) FORMIC ACID.

C.		*W.*	*M*	*E*	*N*	*T.*	$T_{av.}$	T_c
	cathode	110.415	0 024070	0 001267		0 208		
0.2494					0 006096		0 211	
	anode	109 435	0 021291	0 001309		0 215		
	cathode	127 032	0 028133	0.001392		0 219		
0.2541					0 006352		0.215	
	anode	114.168	0 022690	0 001344		0.212		
	cathode	115 490	0 025719	0 001384		0 217		
0.2544					0 006370		0 214	
	anode	127 355	0 025488	0 001347		0 211		
	cathode	123 857	0 027847	0.001330		0 212		
0.2585					0 006266		0.216	
	anode	117.449	0.023772	0.001373		0.219		
								0.214
	cathode	106.845	0.037276	0.001806		0.191		
0.3995					0.009246		0.189	
	anode	111.308	0.035240	0.001713		0.188		
								0.189

tions. The data for potassium formate do not show quite as good an agreement when the results for any given concentration are compared with each other; this is doubtless due to the fact that the salt and its solutions in formic acid are extremely hygroscopic and that during the unavoidable manipulations involved more or less water is taken up. The moisture absorbed would increase the conductivity of the solutions and thus give too high a calculated concentration which would cause the transference number at the cathode to appear too high and at the anode too low; in agreement with this assumption we find that in almost all cases where the two values are not practically identical the cathode value is higher than the anode value, if we except the most concentrated solutions. While the data for potassium formate are therefore not quite as reliable as those for the sodium salt, they are nevertheless quite acceptable when it is considered that the total amount of salt transferred is only from 0.001 to 0.003 gram equivalent and that therefore an error of 0.05% in the determinations of the concentration might readily produce an error of from 1 to over 4% in the transference numbers.

If we compare the transference numbers obtained for potassium formate at different concentrations, it is seen that no experimental error of the type described can account for the large and regular change which occurs when the concentration is progressively increased. Potassium formate in (anhydrous) formic acid solutions appears to obey the law of mass action when the degree of ionization is calculated from the conductivities of the solutions on the assumption that the equivalent conductivity for complete ionization is independent of the concentration.[1] In view of this fact one would expect the transference numbers also to be independent of the concentration. The most rational explanation of this discrepancy is to assume that the Hittorf transference number which we have here measured is not the true transference number because of solvation of the ions. The following calculations show that this assumption can account for the change in transference number observed. If we assume that only the potassium ion is solvated, it is clear that the amount of solvent found in the cathode portion is larger and that in the anode portion smaller than it would have been had none of the solvent been transferred. A correction may then be applied in the following manner. If n is the number of molecules of the solvent, formic acid, associated with each molecule of potassium ion, x the "true" transference number, and N the number of Faradays passed through the solution, the weight of formic acid in g. carried to the cathode is $46.x.n.N$. If W is the corrected weight of solvent in the cathode portions, f the number of equivalents of potassium formate contained in one gram of the solvent in the original solution and E the number of equivalents of the salt contained in W g. of the solvent in the cathode portions, we have

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[1] See the earlier papers of the series, *Loc. cit.*

$$x = \frac{E - (W - (46.x.n.N))f}{N},$$

which can readily be solved for x if n, the number of molecules of the solvent associated with each molecule of potassium ion, is known. A similar calculation can be made for the anode portions. In Table IV, the results of such calculations with several values of n are reproduced. It will be seen that the assumption that the potassium ion is solvated is sufficient to account for the fact that the Hittorf transference numbers change with the concentration as they do, since the "true" transference numbers calculated in this way are as nearly constant as they can be expected to be when the various sources of experimental error are considered. The data are not accurate enough to determine accurately the number of molecules of solvent associated with the potassium ion since the calculations with different values of n do not show any great difference in constancy. It is clear, however, if this method of calculation is correct, that the value of n probably is not less than 6 nor greater than 8, a conclusion which is to be subjected to further test and which is of interest in view of Werner's theory of complexes and of the process of ionization.[1] In Table IV, the first column contains the approximate value of the concentrations, Col. 2 the transference number when n is zero—in other words, the Hittorf number—which is included for comparison and the remaining columns give the transference number, x, as defined above, when the value for n is respectively taken to be 5, 6, 7, 8 and 9. At the bottom of each column will be found the difference in *per cent.* between the extreme values of the transference numbers in the column.

TABLE IV.

Transference Numbers.

C.	$n = 0.$	$n = 5.$	$n = 6.$	$n = 7.$	$n = 8$	$n = 9$
0.10	0.269	0.273	0.274	0.275	0.277	0.278
0.20	0.258	0.269	0.271	0.271	0.276	0.279
0.31	0.249	0.264	0.268	0.271	0.276	0.279
0.39	0.244	0.265	0.268	0.274	0.279	0.283
Difference...	10%	3%	2%	1.5%	1%	1.7%

We may now use the transference numbers of these two salts to calculate for one of them the conductivity at infinite dilution without the use of conductivity data for that salt. Thus, the conductivity at infinite dilution for the sodium salt obtained by extrapolation of the conductivity data, is 66.225.[2] The transference number, at 0.25 N, was found to be

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[1] See also Kendall and Booge, THIS JOURNAL, 39, 2323 (1917).

[2] See the sixth paper of this series, *Loc. cit.*

0.220.[1] By the usual method of calculation we derive 14.6 for the equivalent conductance of the sodium ion and 51.6 for that of the formate ion. From the latter and the transference number of potassium formate at 0.25 *N*,[2] we obtain 17.5 for the equivalent conductance of the potassium ion. Since the corresponding value for the formate ion is, as just stated, 51.6, the equivalent conductance of the potassium formate at infinite dilution should be the sum of these two, namely, 69.1, which proves to be practically identical with the value 68.92 derived in our previous work by extrapolation from conductivity data. We have therefore shown that the calculation of both the conductivity at infinite dilution and the ionization constant from the conductivity data alone introduced no error into our conclusion that there is a real agreement between the behavior of the alkali metal formates and the demands of the mass law and this chapter of our work on formic acid as a solvent is therefore considered complete.

One other point of interest appears from the data presented. It is seen that the equivalent conductance of the formate ion is very much greater than that of the positive ions combined with it in the salt molecules. This is like the behavior of the hydroxide ion in aqueous solutions to which the formation in formic acid solutions is analogous. The same explanation as the one usually given for the great mobility of the hydrogen and hydroxide ions in aqueous solutions may be applied to the great relative mobility of the formate ion in our solutions. On the other hand, since some evidence has been presented which tends to show that the positive ions are apparently much more extensively solvated than is the formate ion, we may ascribe to this difference the difference in the mobilities of the ions.

The transport experiments on solutions of calcium formate were included in order to throw further light on the questions raised by the anomalous behavior of the alkaline earth formates which, in formic acid solutions, obey the law of mass action as developed for uni-univalent salts in moderately concentrated solutions but not in dilute solutions.[3] This behavior suggests the possibility that in the range of concentration for which this law is applicable, ionization into an intermediate ion, *e. g.*, $CaOCHO^+$, exclusively takes place. This question can be answered by the transference data. It can be shown, if V represents the speed of diffusion of the formate ion in centimeters per second under a potential gradient of one volt per cm., λ_0 represents the equivalent conductivity calculated on the assumption that the equivalent weight of calcium formate is $^1/_2$ its molecular weight, n_1 is the transference number of the formate ion if the salt dissociates into formate ion and $CaOCHO^+$ and n_2 the transference number if the salt dissociates into formate and calcium ions, that the two following equations are correct provided either the one or the other mode of ionization occurs exclusively:

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[1] The true transference numbers obtained as described above ought perhaps to be used for these calculations. The results if this is done do not differ materially from those given in the text and since the value of the "true transference numbers" as well as the theory upon which they were calculated need further verification, it has been thought best to proceed as has been done in the text.

[2] This value is obtained by graphical interpolation from the data of Table II, since no data are available for this concentration. The interpolation is over a very short interval.

[3] Schlesinger and Mullinix, THIS JOURNAL, [illegible]

$$2\lambda_0 = \frac{FV}{n_1} \quad (1), \qquad \text{and} \qquad \lambda_0 = \frac{FV}{n_2} \quad (2)$$

Equation 1 applies to ionization into the intermediate ion and Equation 2 to ionization into the simple ions. If dissociation into the intermediate ion occurs, the change in concentration of formate ion constituent at the anode is due (*a*) to formate ion discharged at the electrode, (*b*) to formate ion carried into the anode portion, and (*c*) to calcium formate ion carried from the anode portion. If S_0 represents the number of gram equivalents of calcium formate contained in the anode portion before electrolysis, and S_f the number of gram equivalents of the salt in this portion after electrolysis, and N is the number of equivalents of electricity passed,

$$2S_0 - N + Nn_1 - (1 - n_1)N = 2S_f \quad \text{or} \quad n_1 = \frac{N - (S_0 - S_f)}{N}.$$

If, on the other hand, ionization occurs only into the simple ions, the change in the concentration of the formate ion constituent is due only to the formate ion discharged at the anode and the formate ion carried into the anode portion by transference. Hence,

$$2S_0 - N + n_2N = 2S_f \quad \text{or} \quad n_2 = \frac{N - 2(S_0 - S_f)}{N}.$$

In Table III, the data under T and T_{av} represent the fraction $(S_0 - S_f)/N$. Hence n_1 and n_2 become respectively equal to $1 - T$ and $1 - 2T$. Hence, if ionization into the intermediate ion is the exclusive mode of ionization of the salt, $2\lambda_0 = FV/(1 - T)$. FV, the equivalent conductance of the formate ion, has been obtained from the work with sodium and potassium and at 0.25 N has been found to be 51.5 reciprocal ohms. Taking for T, the average value 0.214, $2\lambda_0$ from the equation just given is calculated to be 65. Actually, λ_0 was found by Schlesinger and Mullinix to be 55. Hence the transference data do not support the view that calcium formate dissociates exclusively as a uni-univalent salt. On the other hand, if the salt is assumed to ionize exclusively into the simple ions we would have the equation $\lambda_0 = FV/(1 - 2T)$. Calculated as before, we get 90 for the value of λ_0. This agrees just as little with the experimentally determined value, 55. Hence the transference data do not decide the question raised, unless we assume that they may be taken to indicate that both modes of dissociation occur—a conclusion already tentatively suggested in the discussion of the work of Schlesinger and Mullinix referred to above.[1]

Summary.

1. The transference numbers of solutions of sodium, potassium and calcium formates in (anhydrous) formic acid have been measured. From the data for the first two salts the equivalent conductance of the formate ion has been calculated and has been found to be 51.5, whereas the corresponding value for the sodium ion is only 14.6 and for the potassium ion 17.5 reciprocal ohms. The significance of these data has been discussed.

2. The transference number of the potassium ion was found to change with the concentration. This is tentatively explained on the assumption that the ion is solvated and a method for calculating the extent of solvation from the transference numbers is suggested. The results so far available indicate that if the assumptions made in the calculations prove to be correct, each potassium ion is combined with from 6 to 8 molecules of formic acid—a finding which is of special interest when viewed in the light of Werner's theory of complex ions and of ionization in general.

3. The transference numbers obtained for calcium formate do not substantiate the view that calcium formate in formic acid solutions ionizes either entirely as a uni-univalent salt nor entirely as a uni-bivalent salt. It is therefore possible that both modes of ionization occur.

CHICAGO, ILLINOIS

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[1] Two points are to be noted in connection with the calculations upon which these conclusions are based. In the first place the concentration 0.25 equivalent for calcium formate should really be compared with the concentration 0.125 N for sodium or potassium formate when the assumption is made that the calcium salt yields only two ions. Or it would be possible in order to avoid confusion to use the "true transference numbers" calculated for potassium formate. Neither of these alternative methods of calculation produces enough change in the results to influence the conclusions and they have therefore not been given in the text. In the second place it must be borne in mind that the "experimental" value for the equivalent conductance of calcium formate at infinite dilution is a value obtained from the data for the conductivity of that salt in solutions more concentrated than 0.1 equivalent and is based on the assumption that the salt obeys the mass law as derived for uni-univalent salts to infinite dilution. As a matter of fact, the salt does not obey this law below the concentration mentioned (see the fourth paper of the series), hence the value of the conductivity at infinite dilution is a fictitious one which has a meaning only if the salt ionizes into two ions only in the range of concentration for which the mass law holds in the form mentioned. Nevertheless, the use of this fictitious value for the purpose for which it is employed in the text is logical as can readily be understood.

[CONTRIBUTION FROM THE OTHO S. A. SPRAGUE MEMORIAL INSTITUTE, RUSH MEDICAL COLLEGE.]

THE VOLATILITY WITH STEAM OF LOWER FATTY ACIDS IN DILUTE AQUEOUS SOLUTIONS.

BY EDGAR J. WITZEMANN.

Received August 4, 1919.

In some tests of the volatility of the lower α-hydroxy aliphatic acids in dilute aqueous solutions of formic, acetic, propionic or butyric acids, it was again observed[1] that the behavior of the fatty acids in this respect is contrary to the laws of simple mixtures. The 4 fatty acids in dilute aqueous solutions show an increasing volatility with increasing molecular weight. It is proposed here to give briefly a few experimental data and to indicate how these relationships, which are commonly stated to be abnormal, are to be expected on the basis of existing knowledge of the molecular state and hydration of these acids in aqueous solution.

The experiments were done as follows: 2 g. of formic acid (by titration) and the corresponding molecular amounts of the 3 other acids, were each made up to 200 cc. with water. Five cc. of the solutions were pipetted off and titrated with 0.1 *N* sodium hydroxide solution in order to confirm *the concentration of the solution. The remaining* 195 *cc. was* transferred to a common distilling flask (500 cc.) and distilled off slowly in 20 cc. fractions correct to within one drop. The receiver (a calibrated test-tube) was emptied and rinsed. The fractions were then titrated separately with 0.1 *N* sodium hydroxide solution. Typical data are given in the table.

TABLE I.

Relative Volatility of Lower Fatty Acids. (Cc. 0.1 *N* NaOH.)

	Fraction Cc.	Formic Cc.	Acetic Cc.	Propionic Cc.	Butyric Cc.
	5	10.80	10.82	10.78	10.81
1	20	16.70	29.33	52.87	81.92
2	20	19.07	30.85	52.10	71.35
3	20	20.36	32.36	50.10	62.98
4	20	22.65	33.80	47.94	53.77
5	20	24.40	35.63	45.60	44.62
6	20	28.48	38.40	43.00	36.30
7	20	33.76	41.45	39.90	28.39
8	20	42.17	46.70	36.60	20.34
9	20	59.45	56.00	33.03	13.36
Residue		155.88	79.05	24.40	6.58
Total		422.92	423.57	424.54	419.61
Calculated		421.20	421.98	420.42	421.59

The above results are given graphically in Fig. 1.

It appears clearly that there is a gradually increasing volatility of these 4 acids of the aliphatic series with increasing molecular weight, although the boiling points of the acids rise gradually from 101° for formic to 162° for butyric acid. Thus the first fractions contain 3.94% of the formic, 6.92% of the acetic, 12.4% of the propionic, and 19.5% of the butyric acid used, respectively. For the last fractions this order is reversed as shown, and the acid remaining in the distilling flask is as follows: formic acid 36.8%, acetic 18.6%, propionic 5.7%, butyric 1.4%, respectively, of the acid taken.

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[1] Duclaux, *Ann. chim. phys.*, 2, 289 (1874); *Ann. inst. Pasteur*, 9, 265 (1895); cf. also Upson, Plum and Schott, THIS JOURNAL, 39, 731–42 (1917).

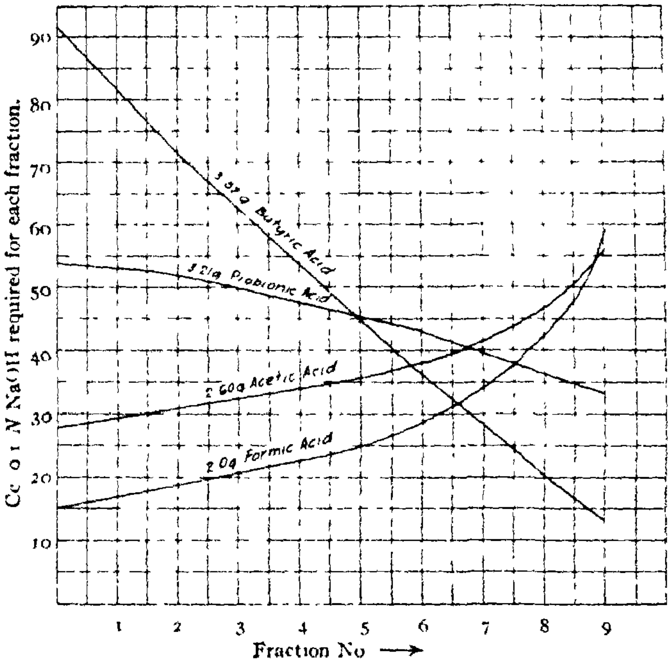

Fig 1.—Relative volatility of the lower fatty acids from boiling aqueous solutions.

The interpretation of these data on the basis of existing knowledge may be briefly stated as follows:

(1) That along with their clearly demonstrated powers of molecular association[1] these 4 acids form hydrates with water.

(2) The hydration, as well as the molecular association of these acids, varies in amount and stability.[2]

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[1] Jones, *Carnegie Inst Publications*, 1915, 210, cf. summary and list of earlier publications at the end. Turner, "Molecular Association," Longmans, Green & Co. (1915).

[2] Cf. Turner, *Loc. cit* for review, Roscoe, *Ann.*, 125, 320 (1863); Peddle and Turner, *J. Chem. Soc.*, 89, 1439 (1907); Colles, *Ibid.*, 89, 1246 (1906), Jones, *Loc. cit.*, p. 148.

(3) The hydrates of greatest stability appear to occur with formic acid (cf. Roscoe, Colles) and this stability appears to diminish with increase in the molecular weight of the 4 fatty acids. It seems evident that this greater stability is due to affinities of the carboxyl group and that the diminishing stability is associated with the increasing hydrocarbon function.[1]

(4) That the hydrates of these acids presumably have the power of lowering the partial vapor pressure of the acid in dilute solutions was definitely established, at least for formic acid, by Roscoe.[2]

(5) It is because of this capacity of the hydrates to lower the partial vapor pressure of the acid that the volatility of these acids in dilute aqueous solution presents a reverse picture as compared with what would be expected if the solutions were simple physical mixtures of the two ingredients. When the decreasing stability of the hydrates at the boiling point of the mixture is considered it appears that the behavior of these acids from the standpoint of simple mixtures tends to become less anomalous on *passing from formic to butyric acid. Accordingly, hydration phenomena* probably have less influence on the volatilization of higher fatty acids (stearic acid) with steam than on those here discussed.

(6) The behavior of dilute solutions of these acids on distillation apparently constitutes evidence of hydration of these compounds since it agrees with all the other data on this subject.

Of the above statements (5) and (6) are perhaps novel.

The Effect of Neutral Salts.

From the existing data regarding the effects of salts on the hydration of another salt in the same solution[3] as well as from Kolossovsky's[4] observations of the influence of salts on the partition of acetic acid between ether and water, the addition of a neutral salt, to such solutions as were used above should produce an increase in the volatility of the fatty acid. This increase in volatility should be greater the greater the concentration of the salt used. That this is true is shown by the data represented in Fig. 2, which were obtained by the same method used above, except that the acetic and formic acids used were weighed. In a 0.5 *M* solution of magnesium chloride (III) the 15 cc. of residue remaining in the distilling flask contains no acetic acid. In (II) this residue consumes 22.65 cc. of 0.1 *N* sodium hydroxide solution, and in (I) it requires 55.75 cc.

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[1] This statement is also supported by Auwer's generalizations on the relation of constitution of solvent and solute to the molecular weight of the latter (*Z. physik. Chem.*, **15**, 33 (1894); **18**, 595 (1895); **30**, 529 (1899); **42**, 513, 542 (1903)) provided the reasonable assumption is made that the ethyl and propyl groups come first beyond the methyl group in this series.

[2] *Loc. cit.*

[3] Jones and Stine, *Am. Chem. J.*, **39**, 313 (1908).

[4] *Bull. Soc. chim. belg.*, **25**, 183 (1911); *Bull. Soc. chim.*, [4] **9**, 632 (1911).

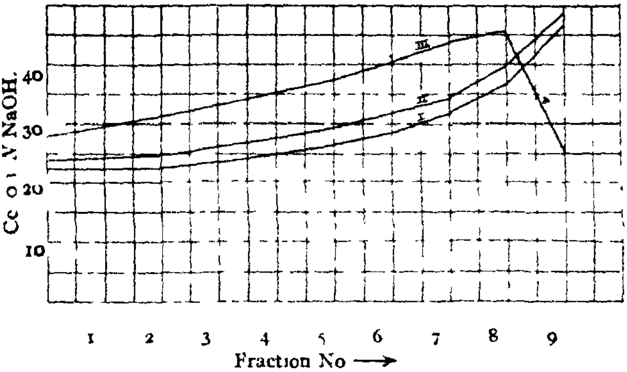

Fig 2.—Effect of dissolved magnesium chloride on the volatility of acetic acid from boiling aqueous solutions

2 0 g. acetic acid in 200 cc { I—H_2O, II—0 1 *M* $MgCl_2$, III—0 5 *M* $MgCl_2$.

In Fig. 3 similar results for formic acid are given.

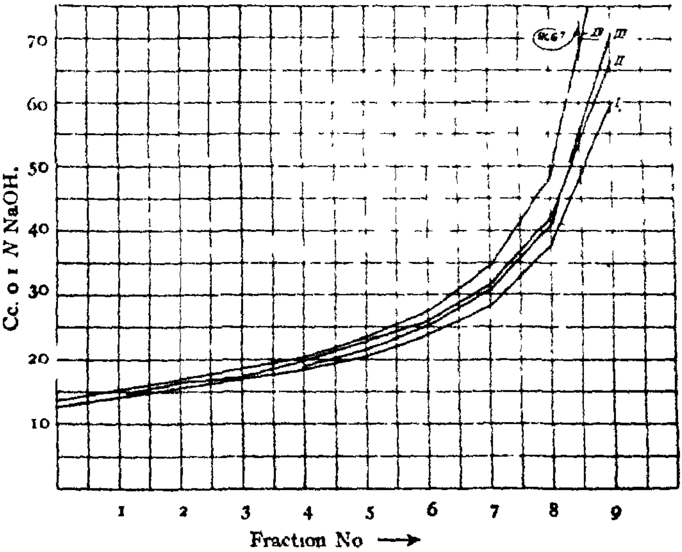

Fig 3.—Effect of dissolved potassium and magnesium chlorides on the volatility of formic acid from boiling aqueous solutions.

2 g formic acid in 200 cc. { I—H_2O. II—0 1 *M* $MgCl_2$. III—0.5 *M* KCl. IV—0.25 *M* $MgCl_2$.

That this increased volatility is not solely a function of the concentration of the salt is suggested by the results for (II) and (III) in Fig. 3. For (III), in which the molecular salt concentration is 5 times greater than in (II), the increase in volatility over (I) averages less than for (II). This apparently indicates that 5 molecules of potassium chloride have a little less positive influence on the volatility of formic acid in this solution than one molecule of magnesium chloride. In experiments with acetic acid, not described here, in a 0.5 *M* potassium chloride solution, the volatility was just a little greater than in a 0.1 *M* magnesium chloride solution.

These results are relatively just what would be expected from our knowledge of the hydration of these salts and thus give further confirmation to the interpretation of the volatility of these acids given above.

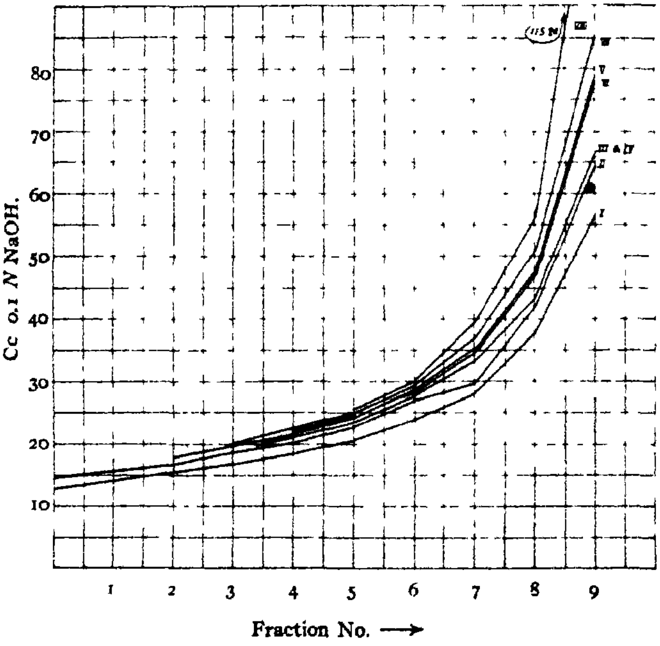

Fig 4.—Influence of dissolved salts (0.25 *M*) on volatility

2.0 g. formic acid in 200 cc
- I—H_2O.
- II—KCl
- III—NaCl sol.
- IV—$BaCl_2$ sol.
- V—$SrCl_2$
- VI—$CaCl_2$.
- VII—$MgCl_2$.
- VIII—$AlCl_3$.

It was of interest to learn whether these relations could be extended in the manner suggested by the deductions of Poma and Albonico[1] regarding the neutral salt effect on the hydrolysis of esters. If their deductions were applicable here equimolecular amounts of metallic salts such as chlorides, for instance, should produce an increasing volatility with the decreasing electro-affinity of the metallic ion of the added salt. Experiments with 0.25 *M* solution of the chlorides of potassium, sodium, barium, strontium, calcium, magnesium, aluminum, manganese, iron and copper were carried out. The volatility was, slightly and progressively, a little increased for each member of this series over the preceding member up to and including aluminum, except in the case of strontium and calcium, for which the order given above should be reversed. The solutions of manganese, iron and copper chlorides showed anomalies and give increases in volatilities lower than aluminum chloride.

Part of the results are given in graphic form in Fig. 4. The results for sodium and barium chlorides are so nearly alike that the results for sodium chloride only were plotted (Curves III and IV)

CHICAGO, ILL.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA.]

THE DEGREE OF IONIZATION OF VERY DILUTE ELECTROLYTES.

BY GILBERT N. LEWIS AND GEORGE A. LINHART.

Received August 16, 1919

The ionic theory in its earlier days would have suffered greater criticism than it received if it had been generally known how great were the discrepancies between the actual behavior of electrolytes and that which was calculated so confidently from the various equations in common use. The failure of the mass law for strong electrolytes was recognized, but in the case of uni-univalent electrolytes, which were most commonly studied, this could be attributed to minor errors in the measurement of conductivity or in Kohlrausch's law of the constancy of ionic mobilities. However, as quantitative data accumulated regarding electromotive force, freezing points, solubilities and the like, it became increasingly evident that the equations generally employed lead to errors which were never trivial and which in some cases became enormous.

The equations in question were based in part upon a safe foundation of thermodynamics, but also in part upon two assumptions of doubtful validity. The first of these assumptions was that the concentration of the ions could be obtained from conductivity ratios. The second was the assumption that the ions and undissociated parts of an electrolyte follow the laws of the so-called ideal solutions. The discrepancies to which we have referred show that one at least of these assumptions must be incorrect. It was therefore proposed by Lewis to investigate, for each molecular species yielded by an electrolyte, that which might have been termed the effective thermodynamic concentration, and which he called activity.[1] This is a quantity which, at infinite dilution, may be taken as equal to the concentration, but which deviates from the latter when the solution ceases to behave as an ideal solution. With changing concentration the activity of any dissolved substance is related to the free energy by the equation,

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[1] *Atti accad. Lincei*, **24**, I, 747, 979, II, 43 (1915).

$$dF = RTd\ln a, \tag{1}$$

where F and a are respectively the free energy and the activity.

The amount of experimental material for such a calculation was at first very meagre, but by summarizing all available information regarding uni-univalent electrolytes Lewis[2] was able to show that in all cases of moderately dilute solutions the ion activity is lower than the ion concentration as determined by the familiar conductivity method In other words, the ion activity divided by the total concentration of the electrolyte, which he called the corrected degree of dissociation, is less than λ/λ_0. Recent studies of the electromotive force of concentration cells and of the freezing points of salt solutions have added greatly to the material available for such calculations. In this paper we will consider only the latter type of measurements and will describe a simple method of calculating the ion activities from freezing-point data.

In the paper just mentioned an equation was developed which permits in the case of dilute solutions[3] the calculation of the free energy of dilution from freezing-point data. This equation is

$$\int dF = 55.5 \frac{\Delta H}{T} \int \frac{d\theta}{c}, \tag{2}$$

where F is the partial molal free energy of the solute; ΔH the molal heat of fusion of ice; T the temperature of fusion, 273.1°; c the number of mols of solute in 1000 g. or in 55.5 mols of water; and θ is the lowering of the freezing point. This equation by graphical integration gives the free energy of dilution over any range of dilute solutions for which accurate freezing-point measurements are available. The method is, however, time consuming and does not lend itself to extrapolation to high dilutions where accurate experimental determinations are no longer possible. In order to obviate these difficulties we have sought a satisfactory empirical equation connecting c and θ.

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[1] Lewis, *Proc Amer. Acad.*, 43, 259 (1907)

[2] Lewis, THIS JOURNAL, 34, 1631 (1912).

[3] The interpretation of freezing-point data in concentrated solutions presents a more complicated problem See Rodebush, THIS JOURNAL, 40, 1204 (1918).

Before discussion the empirical equation we may combine Equations 1 and 2, and find

$$RT\int d\ln a = 55.5\,\frac{\Delta H}{T}\int\frac{d\theta}{c}. \qquad (3)$$

If the solute is ionized its activity is proportional to the product of the activities of the ions into which the molecule dissociates. Thus in the case of a binary electrolyte if a_1 is the activity of one ion and a_2 of the other, then

$$RT\int d\ln(a_1a_2) = 55.5\,\frac{\Delta H}{T}\int\frac{d\theta}{c} \qquad (4)$$

Now if we write $x^2 = a_1a_2$ we may regard x as the activity of either ion as long as we assume the two to be identical, which in the case of uni-univalent electrolytes is probably justifiable up to a concentration of nearly 0.1 molal. More generally x is the mean activity of the ions (geometrical mean). Substituting in Equation 4,

$$RT\int d\ln x^2 = 2RT\int d\ln x = 55.5\,\frac{\Delta H}{T}\int\frac{d\theta}{c}, \qquad (5)$$

or

$$\int d\ln x = \frac{55.5\,\Delta H}{2RT^2}\int\frac{d\theta}{c} = \frac{1}{2\lambda}\int\frac{d\theta}{c}, \qquad (6)$$

where λ, which we have written in place of $\frac{RT^2}{55.5\,\Delta H}$, is at once recognized as the theoretical molal lowering, namely 1.858° per mol of solute in 1000 g. of water.[1]

The treatment of a bi-bivalent salt is identical with that just given for uni-univalent salts. In both cases $x = c$ at infinite dilution, and if we define the thermodynamic, or the corrected, degree of dissociation by the equation $\gamma = x/c$, then γc is the activity of either ion as long as the two activities may be considered as identical. In dealing with an electrolyte of mixed type the matter is a little nore complicated. If, in general, a molecule of the electrolyte yields n_1 molecules of the first ion and n_2 of the second, and if we are to define the quantity x so as to satisfy conditions similar to those above, we must write

$$x = \left[\left(\frac{a_1}{n_1}\right)^{n_1}\left(\frac{a_2}{n_2}\right)^{n_2}\right]^{1/n}, \qquad (7)$$

where $n = n_1 + n_2$. Thus for $La_2(SO_4)_3$, $n_1 = 2$, $n_2 = 3$, and $n = 5$. We may still call $x/c = \gamma$, the corrected degree of dissociation.

Since the activity of an electrolyte is still proportional to the product of the ion activities raised to the appropriate powers, a is also proportional to x^n and we have in general

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[1] In the older literature this constant is given as 1.85°. A critical study of the data for the heat of fusion of ice (Lewis, THIS JOURNAL, 30, 681 (1908)) led to the above value, which is now very [illegible]

$$\int d\ln x = \frac{1}{n\lambda}\int\frac{d\Theta}{c}. \qquad (8)$$

A General Equation for the Freezing-Point Lowering of Dilute Strong Electrolytes.

If n is the number of molecules yielded by the complete ionization[1] of one molecule of the solute the quantity $(n\lambda - \Theta/c)$ approaches zero as c approaches zero. If we plot the logarithm of this quantity against the logarithm of c we obtain a most striking result. The curves for all types of electrolytes approach straight lines as the dilution increases. The more accurate the results, the closer is the agreement with this law, which appears to be one of universal validity. The principle may be expressed in the equation

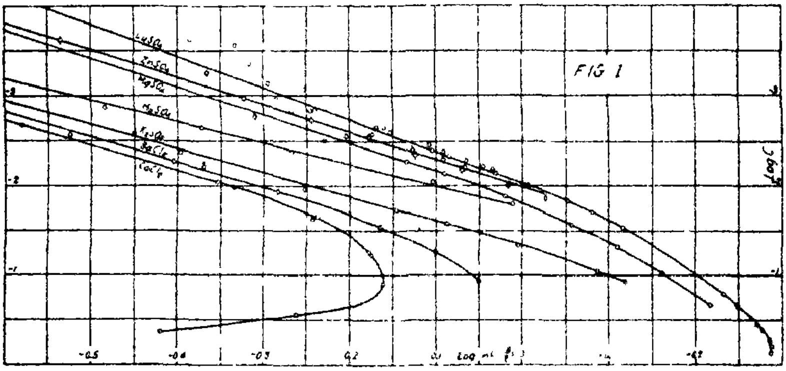
FIG 1

$$\log(n\lambda - \Theta/c) = \alpha \log c + \log \beta, \qquad (9)$$

where α and $\log \beta$ are constants characteristic of the particular electrolyte. In the plot just referred to α is the slope of the line, and $\log \beta$ the inter-

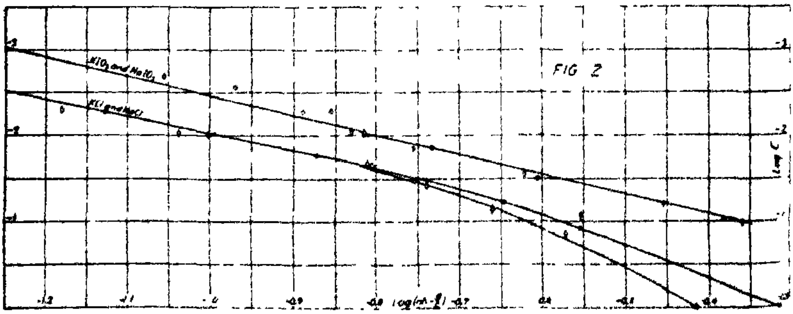
FIG 2

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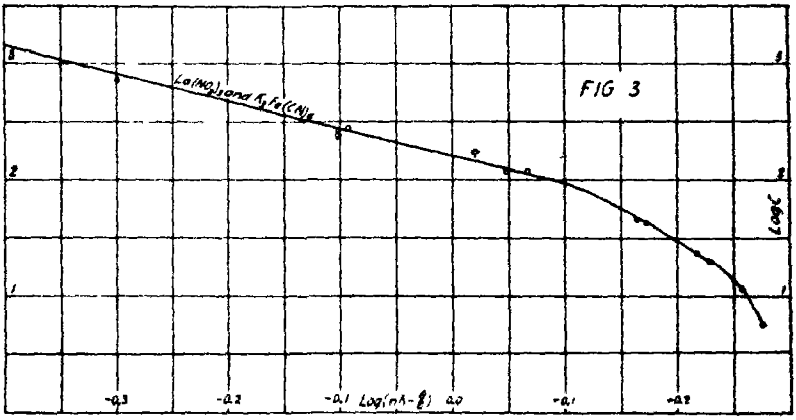
[1] In a thermodynamic calculation such as is to be made here it is of course a matter of choice whether possible intermediate ions are to be considered. For our present purpose it will be more convenient to leave them out of consideration.

section of the line with the axis of $(n\lambda - \Theta/c)$. By combining the last two terms of (9) and taking the antilogarithms, we may put our equation in the form

$$n\lambda - \Theta/c = \beta c^{\alpha}. \qquad (10)$$

We have collected in the following tables the freezing-point data of a number of experimenters who have succeeded in attaining a high degree of accuracy. The values for potassium chloride are due to L. H. Adams,[1] and those for sodium chloride to Harkins and Roberts,[2] except that the values at molal concentration for these two salts are those obtained by Rodebush.[3] The values for sulfuric acid, cadmium and zinc sulfates, and most of those for cupric sulfate, are taken from Hausrath.[4] The remaining points for cupric sulfate, taken from Bedford[5] and from Pick-



UNI-UNIVALENT ELECTROLYTES.

TABLE I. KCl.

$\alpha = 0\ 535,\ \beta = 1\ 223$

c	Θ	Θ calc — Θ obs
0 00506	0 0184	+0 000040
0 00963	0 0348	0 000000
0 01648	0 0590	0 000000
0 03170	0 1122	
0 05818	0 2031	...
0 1168	0 4014	.
1.000	3 23	. .

TABLE II. NaCl.

$\alpha = 0\ 535;\ \beta = 1\ 223.$

c	Θ.	Θ calc. — Θ obs.
0 005132	0 0187	—0 000004
0 009544	0 0346	—0.000104
0 009604	0 0347	+0 000012
0 02012	0.0716	+0.000126
0 02120	0.0755	—0.000018
0 03516	0 1243	. ....
0 06534	0.2286	......
(0 08360)	(0.2872)	......
(0 13600)	(0 4689)	......
1 000	3.33	......

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[1] L. H Adams, THIS JOURNAL, 37, 494 (1915).

[2] Harkins and Roberts, *Ibid*, 38, 2676 (1916).

[3] Rodebush, *Ibid*, 40, 1204 (1918).

[4] Hausrath, *Ann phys.*, [4] 9, 522 (1902).

[5] Bedford, *Proc Roy Soc London*, 83A, 454 (1909).

TABLE III. KIO$_3$.

$\alpha = 0.442$, $\beta = 1.1957$

c	θ	θ calc — θ obs
0.00274	0.00990	+0.000038
0.00506	0.01815	+0.000071
0.00903	0.03220	−0.000008
0.01358	0.04810	−0.000080
0.03244	0.1125	−0.000517
0.09380	0.3085	+0.000066

TABLE IV. NaIO$_3$

$\alpha = 0.442$, $\beta = 1.1957$.

c	θ.	θ calc — θ obs
0.00212	0.00770	+0.000008
0.00499	0.01785	+0.000114
0.00929	0.03310	0.000000
0.01502	0.05300	−0.000009
0.02868	0.0997	−0.000295
0.06329	0.2129	0.000000
0.10100	0.3317	0.000000

UNI-BIVALENT ELECTROLYTES

TABLE V K$_2$SO$_4$

$\alpha = 0.374$, $\beta = 3.187$

c.	θ	θ calc θ obs
0.00274	0.0143	+0.000011
0.00404	0.0209	−0.000021
0.00618	0.0318	−0.000294
0.01039	0.0521	−0.000192
0.01756	0.0854	+0.000135
0.02608	0.1241	0.000000
0.04547	0.2085	
0.08899	0.3874	
0.12050	0.5120	

TABLE VI H$_2$SO$_4$

$\alpha = 0.417$, $\beta = 5.404$

c	θ	θ calc – θ obs
0.0001150	0.000564	+0.000063
0.0003315	0.00158	+0.000204
0.0006458	0.00318	+0.000257
0.001339	0.00703	−0.000024
0.002243	0.01155	0.000000
0.004175	0.02102	−0.000041
0.00942	0.04507	+0.000164
0.01646	0.07569	0.000000

TABLE VII BaCl$_2$.

$\alpha = 0.364$, $\beta = 2.660$

c.	θ	θ calc — θ obs
0.00273	0.0144	−0.000030
0.00534	0.0276	−0.000000
0.01142	0.0577	0.000000
0.02982	0.1458	
0.05611	0.2682	
0.11358	0.5330	

TABLE VIII CoCl$_2$

$\alpha = 0.362$, $\beta = 2.456$

c	θ	θ calc — θ obs
0.00173	0.00930	−0.000082
0.00209	0.01110	0.000000
0.00892	0.04575	0.000000
0.01008	0.05149	+0.000019
0.02251	0.1126	
0.02375	0.1188	
0.05475	0.2688	
0.05973	0.2933	
0.1256	0.6134	. .
0.2772	1.3932	. .
0.4217	2.1899	..... .

BI-BIVALENT ELECTROLYTES

TABLE IX. MgSO$_4$

$\alpha = 0.293$, $\beta = 3.404$

c.	θ.	θ calc — θ obs
0.00320	0.01000	−0.000131
0.00535	0.01595	0.000000
0.00746	0.02165	+0.000029
0.01310	0.03615	−0.000000
0.02668	0.06730	
0.04878	0.1182	.
0.09566	0.2163	......
0.2210	0.4566	... ..

TABLE X CdSO$_4$.

$\alpha = 0.325$, $\beta = 4.421$.

c	θ.	θ calc — θ obs.
0.000239	0.00084	−0.000032
0.000704	0.00236	−0.000038
0.001511	0.00482	−0.000014
0.002685	0.00819	+0.000053
0.006560	0.01858	−0.000015
0.01151	0.03094	. ...
0.01950	0.04957	......
0.03120	0.07556	......

Table XI. $CuSO_4$.

$\alpha = 0.2840$, $\beta = 3.760$

c	θ	θ calc — θ obs
0.000233	0.00077	+0.000015
0.000286	0.00093	+0.000027
0.000442	0.00143	+0.000027
0.000735	0.00236	+0.000016
0.000843	0.00266	+0.000048
0.001051	0.00336	−0.000018
0.001467	0.00461	−0.000023
0.001520	0.00483	−0.000086
0.001521	0.00479	−0.000043
0.002229	0.00677	+0.000036
0.002328	0.00705	+0.000036
0.002619	0.00789	+0.000022
0.002653	0.00807	−0.000061
0.003441	0.01011	+0.000093
0.003999	0.01172	+0.000012
0.004316	0.01255	+0.000031
0.004810	0.01392	−0.000014
0.005433	0.01551	+0.000034
0.006097	0.01718	+0.000093
0.006670	0.01859	+0.000153
0.007350	0.02046	0.000000
0.010000	0.02700	0.000000
0.0150	0.03885	
0.0200	0.0502	
0.0300	0.0726	
0.1658	0.3344	
0.2333	0.4540	
0.3468	0.6410	
0.4081	0.7422	
0.5290	0.9409	
0.6236	1.1071	
0.7453	1.3258	

Table XII $ZnSO_4$

$\alpha = 0.3250$; $\beta = 4.421$.

c	θ	θ calc — θ obs
0.000136	0.00050	−0.000028
0.000236	0.00081	−0.000002
0.000399	0.00139	−0.000046
0.000597	0.00196	+0.000022
0.000916	0.00307	−0.000083
0.001081	0.00350	−0.000002
0.001695	0.00546	−0.000104
0.001853	0.00583	−0.000004
0.002776	0.00858	−0.000074
0.002850	0.00868	+0.000035
0.004019	0.01192	+0.000060
0.004412	0.01309	−0.000044
0.005160	0.01499	+0.000067
0.006259	0.01786	+0.000081
0.006510	0.01862	−0.000034

Uni Trivalent and Tri-Univalent Electrolytes

Table XIII $K_3Fe(CN)_6$

$\alpha = 0.420$, $\beta = 8.531$

c.	θ	θ calc — θ obs
0.00050	0.003675	−0.000130
0.00100	0.00714	−0.000177
0.00200	0.01362	−0.000010
0.00400	0.02656	−0.000198
0.00600	0.03828	+0.000342

Table XIV. $La(NO_3)_3$.

$\alpha = 0.420$, $\beta = 8.531$.

c.	θ	θ calc — θ obs.
0.00132	0.00915	−0.000030
0.00354	0.02345	+0.000038
0.00806	0.05090	+0.000074
0.00857	0.05370	+0.000085
0.02222	0.1328	....
0.02360	0.1404	....
0.04337	0.2508	....
0.05119	0.2937	....
0.08661	0.4878	...
0.17486	0.0608	

ering,[1] are not of the highest accuracy, but are given to show the trend of the curve in the more concentrated solutions. The same is true of Bedford's values for potassium ferricyanide. The data for all the remaining salts are taken from Hall and Harkins.[2]

These various values have been plotted in Figs. 1, 2 and 3,[3] and the values of α and of β obtained from the plots are given in the individual tables. The remarkable agreement with the straight line formula is shown not only by the curves but also in the tables, where the difference between the observed values of Θ and those calculated from our formula are given for the more dilute solutions.[4]

Calculation of the Thermodynamic or Corrected Degree of Dissociation.

By rearrangement of Equation 10 we may write

$$\Theta = \lambda n c - \beta c^{\alpha+1}. \tag{11}$$

Differentiating,

$$d\Theta = n\lambda dc - \beta(\alpha + 1)c^{\alpha}dc \tag{12}$$

and dividing both sides by $n\lambda c$,

$$\frac{d\Theta}{n\lambda c} = d\ln c - \frac{\beta(\alpha + 1)c^{\alpha - 1}}{n\lambda} dc. \tag{13}$$

This form of our empirical equation we may now combine with the thermodynamic Equation 8, giving

$$\int d\ln x = \int d\ln c - \frac{\beta(\alpha + 1)}{n\lambda}\int c^{\alpha - 1}\, dc. \tag{14}$$

Integrating between c_0 and c

$$\ln x - \ln x_0 = \ln c - \ln c_0 - \frac{\beta(\alpha + 1)}{n\lambda\alpha}(c^{\alpha} - c^{\alpha}_0). \tag{15}$$

Now if we take one of our limits at infinite dilution, namely, $c_0 = 0$, then $x_0 = c_0$, and

$$\ln x = \ln c - \frac{\beta(\alpha + 1)c^{\alpha}}{n\lambda\alpha} \tag{16}$$

and writing $\gamma = x/c$,

$$\ln\gamma = -\frac{\beta(\alpha + 1)c^{\alpha}}{n\lambda\alpha}, \tag{17}$$

or with common logarithms,

$$\log\gamma = -\frac{\beta(\alpha + 1)c^{\alpha}}{2.303\, n\lambda\alpha} \tag{18}$$

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[1] Pickering, *Ber.*, 25, 1314 (1892).

[2] Hall and Harkins, This Journal, 38, 2658 (1916).

[3] In the figures the plain circles are used to denote KCl, KIO_3, $CuSO_4$, $MgSO_4$, H_2SO_4, K_2SO_4, $CoCl_2$ and $La(NO_3)_3$. The circles with lines drawn through them are used to denote NaCl, $NaIO_3$, $ZnSO_4$, $BaCl_2$ and $K_3Fe(CN_6)$.

[4] At concentration below 0.001 *M* no great weight can be given to any individual measurement, for below this concentration a large percentage error is inevitable even in the most careful work; thus, at 0.001 *M* an error of 0.0001° is an error of 1% to 3%, depending upon the type of electrolyte.

TABLE XV.

	$(10)^{-1}$	$5(10)^{-2}$	$2(10)^{-2}$	$(10)^{-2}$	$5(10)^{-3}$	$2(10)^{-3}$	$(10)^{-3}$	$5(10)^{-4}$	$2(10)^{-4}$	$(10)^{-4}$	$5(10)^{-5}$	$2(10)^{-5}$	$(10)^{-5}$	$5(10)^{-6}$	$2(10)^{-6}$	$(10)^{-6}$	$5(10)^{-7}$	$2(10)^{-7}$	$(10)^{-7}$	$5(10)^{-8}$	$2(10)^{-8}$	$(10)^{-8}$
KCl	....	....	89.0	92.5	94.6	96.7	97.7	98.4	99.0	99.3	99.5	....	....	....	....	....	....	....	....	....	....	....
$NaCl$	....	....	89.0	92.5	94.6	96.7	97.7	98.4	99.0	99.3	99.5	....	....	....	....	....	....	....	....	....	....	....
KIO_3	68.4	75.6	83.0	87.2	90.4	93.5	95.2	96.4	97.6	98.2	98.7	99.1	99.4	99.5	....	....	....	....	....	....	....	....
$NaIO_3$	68.4	75.6	83.0	87.2	90.4	93.5	95.2	96.4	97.6	98.2	98.7	99.1	99.4	99.5	....	....	....	....	....	....	....	....
K_2SO_4	....	....	61.5	68.7	74.9	81.4	85.3	88.5	91.7	93.5	95.0	96.4	97.2	97.8	98.3	98.8	99.1	99.4	99.5	....	....	....
H_2SO_4	....	....	....	61.7	69.6	78.2	83.1	87.1	91.0	93.2	94.8	96.5	97.3	98.0	98.6	98.9	99.2	99.5	....	....	....	....
$BaCl_2$	....	....	....	71.6	77.1	83.0	86.5	89.4	92.3	93.9	95.3	96.6	97.3	97.9	98.5	98.8	99.1	99.4	99.5	....	....	....
$CoCl_2$	....	....	....	73.1	78.4	84.0	87.3	90.0	92.7	94.3	95.5	96.8	97.5	98.0	98.6	98.9	99.2	99.4	99.5	....	....	....
$CdSO_4$	....	....	....	33.8	42.0	52.6	59.8	66.3	73.8	78.4	82.4	86.6	89.1	91.2	93.4	94.7	95.8	96.8	97.5	98.0	98.5	98.8
$ZnSO_4$	....	....	....	33.8	42.0	52.6	59.8	66.3	73.8	78.4	82.4	86.6	89.1	91.2	93.4	94.7	95.8	96.8	97.5	98.0	98.5	98.8
$MgSO_4$	....	....	....	35.0	42.5	52.0	58.6	64.7	71.7	76.2	80.1	84.4	87.1	89.3	91.7	93.2	94.4	95.7	96.5	97.1	97.8	98.2
$CuSO_4$	....	....	....	29.0	36.2	45.7	52.6	59.0	66.6	71.6	76.0	80.9	84.0	86.7	89.6	91.4	92.8	94.4	95.4	96.2	97.1	97.6
$K_3Fe(CN)_6$	....	....	....	57.1	65.7	75.2	80.8	85.3	89.7	92.2	94.1	96.0	97.0	97.7	98.5	98.8	99.1	99.4	99.5	....	....	....
$La(NO_3)_3$	....	....	....	57.1	65.7	75.2	80.8	85.3	89.7	92.2	94.1	96.0	97.0	97.7	98.5	98.8	99.1	99.4	99.5	....	....	....

This equation offers an extremely simple and, we believe, an entirely accurate method of calculating the corrected degree of dissociation of any electrolyte when the constants α and β are obtained from freezing-point measurements. It is of course applicable only in the range of concentration where the linear formula holds. It would be an easy matter to proceed to higher concentrations either by adding a new term with a new constant to our empirical formula, or by plotting the difference between the actual results and those of the linear formula and thus by graphical methods obtain corrections to the results obtained by Equation 18. However, since the deviations from the linear formula appear at about the concentration where the heat of dilution begins to be measurable, and since these heats of dilution, which are necessary for a calculation of the degree of dissociation at other temperatures, are now being subjected to a thorough investigation in this laboratory, we will here content ourselves with the application of Equation 18 to the dilute solutions where the linear formula holds.

The values for the corrected degree of dissociation, which are obtained from Equation 18 by the use of the values of α and β given in the preceding tables, are valid for any ordinary temperatures. The values of the percentage ionization, 100γ, are given in Table XV.

The extraordinary divergence between the degree of ionization obtained by thermodynamic methods and the degree of ionization as it is ordinarily obtained from conductivity data is very pronounced even in these extremely dilute solutions. The greatest divergence occurs in the case of cupric sulfate, where it has already been observed by Lewis and Lacey.[1] In order to show how great this difference is we give in Table XVI our values of γ at 0.01 molal by the side of the values of λ/λ_0 given by Noyes and Falk.[2] Even at 0.001 M λ/λ_0 for cupric sulfate is 86.2, while our value is only 52.6.

TABLE XVI

$c = 0.01\ M.$

	KCl.	$NaCl$.	KIO_3	$NaIO_3$.	K_2SO_4.	$BaCl_2$	$CdSO_4$	$CuSO_4$	$La(NO_3)_3$.
γ........	0.925	0.925	0.872	0.872	0.687	0.716	0.338	0.290	0.571
λ/λ_0....	0.941	0.936	0.928	0.917	0.872	0.883	0.614	0.629	0.802

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[1] Lewis and Lacey, THIS JOURNAL, 36, 804 (1914).

[2] Noyes and Falk, *Ibid*., 34, 474 (1912).

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES, COLUMBIA UNIVERSITY, NO. 329.]

THE TRANSITION OF DRY AMMONIUM CHLORIDE.

BY ALEXANDER SMITH, HERBERT EASTLACK, AND GEORGE SCATCHARD.

Received August 28, 1919.

Introduction and Theoretical Part.

The object of this work was to determine whether dry ammonium chloride changes to a different crystalline form at 184.5° as ordinary ammonium chloride does. The particular interest of this problem lies in its possible bearing on the anomalous vapor density of dry ammonium chloride.

It has been definitely established by the work of Breton Baker[1] that the reaction

$$NH_4Cl \rightleftharpoons NH_3 + HCl$$

does not proceed in either direction in the absence of water as catalyst. As is well known, the vapor density of undried ammonium chloride from 300° to 360° corresponds to a high degree of dissociation,[2] but Baker found by both the Dumas and Victor Meyer methods that the vapor density of the dried substance corresponds closely to NH_4Cl, indicating no dissociation. Since both of these methods require about one atmosphere for operation, we may infer that the vapor pressure of the dried salt is about the same as of the undried. F. M. G. Johnson[3] has measured the vapor pressure of undried and dried ammonium chloride, using the same apparatus and substance for each, and has found that the vapor pressures are the same from 212° to 333°, but that the vapor density of the undried sample at 323° (420 mm. pressure) corresponds to 98% dissociation, while that of the dried substance at the same temperature and with equal pressure corresponds to only 8% dissociation. In his method, the vapor density bulb is at a higher temperature than the bulb containing the solid salt, and he is, therefore, not dealing with the saturated vapor.

The partial pressure of undissociated ammonium chloride vapor in equilibrium with the undried solid must then be small while that in equilibrium with the dried solid is practically the total pressure. Abegg[4] was the first to call attention to this apparent anomaly of the change in the equilibrium point of a heterogeneous equilibrium by a catalyst, and it was at his suggestion that Johnson's work was undertaken. One of the most plausible explanations is that of Wegscheider[5]—that the transition of ammonium chloride does not take place in the absence of water, and that the pressure of NH_4Cl from the unstable form is accidentally the same as the total pressure of NH_4Cl, NH_3 and HCl from the stable form.

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[1] Baker, *J. Chem. Soc.*, **65**, 615 (1894); **73**, 422 (1898).

[2] 65% at 300°, and 63% at 330° for the saturated vapor. (Smith and Lombard, THIS JOURNAL, **37**, 48 (1915).)

[3] Johnson, *Z. physik. Chem.*, **61**, 457 (1908).

[4] Abegg, *Ibid.*, **61**, 455 (1908).

[5] Wegscheider, *Ibid.*, **62**, 607 (1908).

Scheffer,[1] who determined the transition point as 184.5° and measured the heat of transition and the specific heats of the two forms near this temperature, does not consider the thermal effect large enough to explain the phenomenon. Lately, Wegscheider[2] has calculated the heat of transition necessary, and has found that it would be 4 times the value found by Scheffer. His calculations contain many assumptions that are little justified, but the allowance for error is so large that we may agree with his conclusions He then suggests other explanations by transition points, which will be discussed below in relation to our own work.

The transition point was determined by the ordinary thermal method, which depends upon the latent heat of transition. The simplest form of this method is to place a thermometer with its bulb in the center of a few grams of the substance in a test-tube, to place the test-tube in an efficiently stirred bath of relatively large heat capacity, also equipped with a thermometer, and to heat or cool the bath regularly and fairly rapidly, determining the readings of the two thermometers at frequent intervals.

It is customary to plot the temperature as ordinates and the times as abscissas. The curve for the bath is then a nearly straight line. When there is no change of phase in the substance, its curve is very nearly parallel to that of the bath but lies to its right; the perpendicular distance between the two lines represents the temperature gradient between the outer surface of the substance and the thermometer bulb. But near the transition point there is a distinct change in the form of the curve The tendency of the substance is to remain at the constant temperature of the transition point until all is transformed, which would give a horizontal line at the transition point. But the phenomena of superheating or supercooling (which are conspicuous with ammonium chloride) may cause an initial passing of the transition point with a later return toward it, which is illustrated by the cooling curve (Fig. 2). Also, the rapidly changing temperature of the bath may cause a gradual change of temperature during transition. The combination of the two effects is shown by the heating curve (Fig. 1), where the rapid addition of heat had straightened out the sag due to superheating, but the horizontal line is above the true transition point. In any case, the curve approaches the horizontal near the transition point, and then becomes much steeper than the curve for the bath after all the substance is transformed

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[1] Scheffer, *Verslag. Akad Wetenschappen Amsterdam*, 18, 446 (1915); *Ibid.*, 18, 1498 (1916).

[2] Wegscheider, *Z. anorg. Chem* , 103, 207 (1918).

The quantity of substance, the method of packing, and the size of the thermometer bulb also have considerable influence on the shape of the curves. For these reasons this method generally serves only for an approximate determination of transition points. So we have used ordinary, uncalibrated mercury thermometers, and have made no correction for exposed stem.

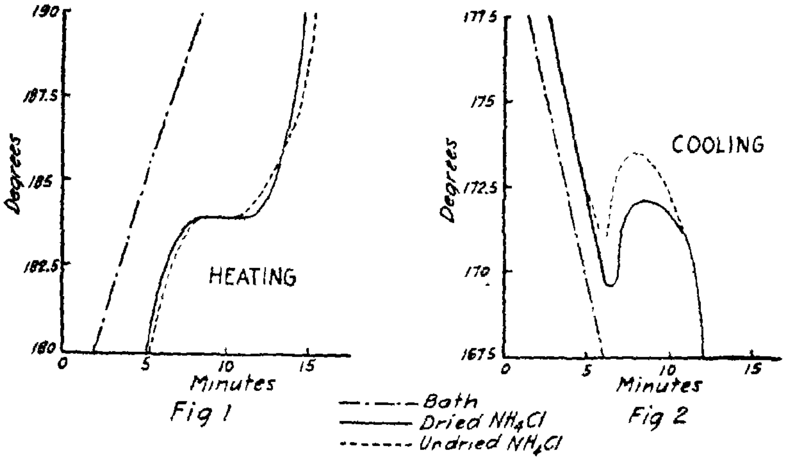

Fig 1

Fig 2

Figs. 1 and 2 are typical heating and cooling curves. They represent the curves for the bath (dot and dash line), for ordinary undried ammonium chloride in a test-tube (dotted line), and for dried ammonium chloride (full line), all determined at the same time. For the last it was necessary to use a more complicated apparatus to obtain and maintain anhydrous conditions. The manipulation and the corresponding table are given under Apparatus No. 4. They show very clearly a transition in the interval 172° to 184° (uncorr.), and show how closely the curves for the dried and the undried salt correspond. Since these determinations are only approximate, it has not been considered worth while to give the curves for the other tables, since a glance at the tables, especially the columns giving the average temperature change per minute, will show that there is an inflection in each case at about this temperature.

Let us compare the thoroughness of our drying with that of the investigators who have found abnormal densities. Baker[1] dried his apparatus by heating in boiling mercury while a current of dry air was passed through. After the introduction of the substance and the phosphorus pentoxide, he let it stand not longer than two weeks at room temperature. Johnson[1] performed the preliminary drying by heating the evacuated apparatus a long time at 300°. After the introduction of the materials, he allowed it to stand 5 weeks at ordinary temperature. We dried the apparatus by heating with a small flame while passing through a current of dry air, and dried the salt after its introduction, at 155° to 165° for 45 days, or 3 years at room temperature, with care to present as large a surface of the solid as possible. Therefore, our material was much more carefully dried than that which did not dissociate. In every case the transition occurred as with the undried ammonium chloride.

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[1] *Loc. cit.*

Wegscheider's first explanation by the failure of dried ammonium chloride to undergo the known transition at 184.5° is rendered improbable by the work of Scheffer and wholly untenable by the fact that it does undergo transition. The fact that the transition occurs at the same temperature also excludes the explanation by another transition at a lower temperature. Our work has no bearing on a second transition at a higher temperature. But if that were to account for the anomaly, the heat of transition would have to be very large, and the fact that Scheffer searched for it in vain strongly indicates its nonexistence.

Wegscheider's third possible explanation is that ordinary α-NH_4Cl is a labile form, which changes to α'-NH_4Cl, but only at higher temperatures and in the presence of moisture. It is the transition α'-NH_4Cl = β-NH_4Cl which occurs at 184.5°, and the α-NH_4Cl does not undergo transition. This would imply a transition from α-NH_4Cl to α'-NH_4Cl, although not necessarily at a definite temperature, and it is impossible as an explanation since dried ammonium chloride does undergo transition at this higher temperature.

His fourth explanation is that the ordinary α-NH_4Cl is stable and undergoes transition at 184.5° to the β-form; but that sometimes in the preparation, a labile α'-NH_4Cl is formed, which does not undergo transition in the absence of moisture and which evaporates without dissociation. Evidently, one may assume any value for the heat of reaction of α'-NH_4Cl = α-NH_4Cl and for the specific heat of the α'-NH_4Cl without contradicting any experimental evidence, if he assumes that all calorimetric measurements have been made on the stable α-form. Similarly, our results would have no bearing on the case, as we did not happen to work with the α'-NH_4Cl.

Wegscheider supports this hypothesis with the statement that Johnson with dried ammonium chloride obtained sometimes undissociated and sometimes dissociated vapor. However, Johnson worked with only one sample of dried ammonium chloride, upon which he made one measurement of vapor density and one ascending and descending vapor-pressure curve. He then allowed moisture to enter and made the same measurements on the undried substance. Moreover, a series of several measurements of the vapor density of ammonium chloride dried 9 months at room temperature gave not a single case of vapor density corresponding to dissociation.[1] The only recorded case of ammonium chloride which had been submitted to an attempt at drying and gave dissociated vapor is that of Gutmann,[2] and Baker[3] claims that he failed to obtain anhydrous conditions. Therefore, there is no justification for attributing the higher vapor density to a rare, accidental form. However, the only experimental answer to this assumption would be to make simultaneous determinations of vapor density and transition point, and so see whether the same sample did undergo transition and give undissociated vapor.

Experimental Part.

Material.

Ammonium Chloride.—For Tubes 2 and 3, "Baker's Special" ammonium chloride was boiled with dil. nitric acid, recrystallized twice from distilled water, sublimed *in vacuo*, recrystallized, resublimed, recrystallized, powdered finely, and dried at 110° for 24 hours. For Tubes 4, 5 and 6, C. P. ammonium chloride was recrystallized from distilled water, dried, sublimed *in vacuo*, ground to a fine powder, and dried at 112° for several hours.

Phosphorus Pentoxide.—Phosphorus pentoxide was sublimed in a current of oxygen over red-hot platinum sponge. It was free from phosphorus trioxide.

Apparatus.

The apparatus, as shown in Fig. 3, consists of a tube E to contain the ammonium chloride and the thermometer bulb and with a long neck for the stem of the thermometer and a side tube with two bulbs (1 and 2) for phosphorus pentoxide, which was also used to make the connection to the pump at C. The thermometers were the ordinary 360° type selected to fit tightly in the neck of the tube.

Preparation of Apparatus.

The apparatus was thoroughly cleaned with sulfuric acid-dichromate mixture and with distilled water, and was finally dried by heating over its entire surface with a small Bunsen flame while drawing through

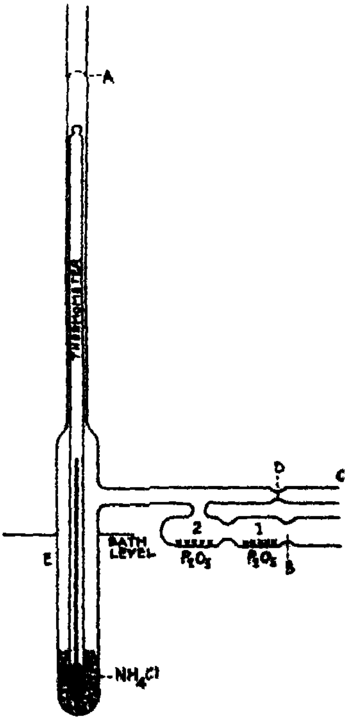

Fig. 3.—Apparatus for the observation of transition of "dry" ammonium chloride.

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[1] Unpublished work of Smith and Lombard.

[2] Gutmann, *Ann.*, 299, 267 (1898).

[3] Baker, *J. Chem. Soc.*, 73, 422 (1898).

a current of dry air. While the tube was still hot, about 15 g. of ammonium chloride was quickly introduced directly from the oven, the carefully cleaned and dried thermometer was put into place, and the tube was sealed off at A. Then 2 or 3 g. of phosphorus pentoxide was put into bulb 1 and the constriction at B sealed off.

Drying and Determination of Transition Point.

Apparatus No. 2.—The apparatus was sealed to the mercury pump at C, exhausted to 0.001 mm. pressure (McLeod gage), and sealed off at D. The bulb E, containing the ammonium chloride, was heated by boiling anisole (154°) while the phosphorus pentoxide bulbs were cooled by immersion in running tap water. After 3 days' heating, about $^1/_3$ of the pentoxide was carefully distilled from bulb 1 to bulb 2.

After nine days' continuous heating, heating and cooling curves were made. The heating was done in a bath of "crisco," in which the Tube E was immersed well above the level of the ammonium chloride. The bath was made of a liter beaker wrapped with asbestos and heated by an electric hot-plate in a room with windows and doors closed to prevent drafts. In each case the temperature of the bath, as determined at frequent intervals, increased regularly but with diminishing rapidity at the higher temperatures.

As indicated in the following table, the transition occurred at 183° and at 175° on heating and cooling, respectively:

Temp Degrees	Heating rate[a] Degrees	Time Minutes	Temp Degrees	Cooling rate Degrees	Time Minutes
175.0		0.0	177.0	.	0.0
180.0	+1.7	3.0	175.0	−1.3	1.5
183.0	0.9	6.3	174.1	0.5	3.25
183.2	0.1	8.0	174.5	+0.2	5.0
183.5	0.2	9.5	174.7	+0.2	6.0
184.0	0.3	11.0	174.0	−0.2	9.0
185.0	0.4	13.5	173.0	0.4	11.6
190.0	1.2	17.6	170.0	0.9	15.0

[a] Rate is average change in degrees per minute since previous reading.

The bulb was further heated at 155-165° in an electrically heated air bath. After 45 days' continuous heating, the transition point was redetermined. Just as the slight drop in temperature from 184° was observed, the tube cracked—presumably due to the expansion of the salt on transition, for during the heating it had become packed in a hard mass between the thermometer and the tube The determination had proceeded far enough to indicate a transition of 184°.

Temp. Degrees	Rate Degrees	Time Minutes.
175.0	..	0.0
180.0	+1.2	4.3
182.0	1.0	6.3
184.0	1.0	8.4
183.8	−0.2	9.2

Tubes 3, 4, 5 and 6 were sealed to the pump at C, exhausted to 0.001 mm., and allowed to stand overnight; they were then heated with a small flame (with the exception of the ammonium chloride and the pentoxide bulbs), again exhausted to 0.001 mm., and sealed off at D. They were similarly heated several times during the next few days. Finally, the pentoxide was carefully distilled into bulb 2.

The ammonium chloride was shaken down so that, with the apparatus on its side, a large surface of the salt over nearly the full length of Tube E was exposed to the drying atmosphere, and the tubes were left thus to dry.

Apparatus No. 6.—After drying 14 months (June 1, 1916 to August 10, 1917), the transition point was determined as before. During the determination, the pentoxide bulbs were cooled in ice-water. The transition occurs regularly at 184–185°. The table includes the temperature of the bath.

Temp of NH_4Cl Degrees.	Rate. Degrees	Temp of bath Degrees	Rate Degrees	Time Minutes
175.0		183		0.0
180.0	+3.3			1.5
182.0	3.0			2.2
183.0	2.5			2.6
184.0	1.1			3.5
184.5	0.5			4.6
185.0	0.7			5.3
186.0	0.8			6.6
190.0	1.9			8.7
193.0	1.8	202	1.8	10.4
194.0	0.5			12.3
193.0	−0.5			14.3
192.0	−1.0	211	1.8	15.3
191.0	−0.9			16.4
190.0	−0.7	.		17.9
189.5	−0.2	219	+1.7	20.1
189.0	−0.3			22.9
189.5	+0.2			25.3
190.0	0.2			27.5
191.0	0.2			33.8
192.0	0.2			38.3
193.0	0.4			40.6
194.0	0.5			42.5
195.0	1.0			43.3
200.0	1.2			47.4
205.0	2.5	..		49.4
215.0	4.0	260	1.3	51.9
240.0	0.5	..		100.8
...	...	...	...	...
...	...	...	...	...

It will be observed that there is a second drop in the temperature at 194°. This is undoubtedly due to distillation of the ammonium chloride and a consequent isolation of the thermometer bulb. At the end of the determination, the salt had entirely distilled into the upper part of the apparatus. The same effect was observed in very carefully evacuated tubes containing ammonium chloride without the addition of phosphorus pentoxide. In 3 cases the distillation occurred at 150, 160 and 167°. This larger thermal effect would of course hide a transition point. The last of these determinations is given in the following table:

Temp of NH₄Cl Degrees.	Rate. Degrees.	Temp. of bath. Degrees	Rate. Degrees.	Time. Minutes	Temp. of NH₄Cl. Degrees.	Rate. Degrees.	Temp. of bath Degrees.	Rate. Degrees.	Time. Minutes
160.0		170	...	0 0	165.9	+0.01	200	+0.7	28.2
165 0	+1 1	181	+2 3	4 7	166 0	0.04	.	...	30.5
167.0	0 5			9 0	166 4	0.06	..		37.2
166.8	—0 05	190	+1 1	13 2	167 0	0 1	210	0.7	43.5
166.5	—0 2		.	14 5	168 0	0 1	...		51.5
166.2	—0 15			16 5	169 0	0 1		.	61.0
166.0	—0 4			17 0	170 0	0 1	217	0 25	72 0
165.8	—0 07			19 7		.	...	..	.

Apparatus No. 5.—Treated exactly as No. 6, it shows the same therma effects—transition at 184–185°, and the distillation commencing at 198.5 instead of at 194°.

Temp of NH₄Cl. Degrees	Rate Degrees	Time Minutes	Temp of NH₄Cl. Degrees	Rate Degrees	Time Minutes	Temp of NH₄Cl Degrees	Rate Degrees	Time Minutes	Temp of NH₄Cl Degrees	Rate Degrees	Time Minutes
173.0	..	0 0	185 0	+1 7	7 0	198 5	±0 0	16 0	200	+0 3	48 4
177.0	+4 0	1 0	187 0	2 2	7 9	198 0	—0 2	18 1	205	0 5	59.5
180 0	3 3	1 9	190 0	3 7	8 7	197 0	—0 4	20 8	210	1 6	62 6
182.0	1 8	3 0	195 0	2 9	10 4	196 6			220	4 3	64 9
182 5	0 5	4 1	196 0	1 2	11 2	197 0		26 7	230	5 9	66 6
183 0	0 6	5 0	198 0	1 0	13 3	198 0	+0 1	37 8	256	3.9	73 3
184 0	0 7	6 4	198 5	0 3	15 0	199 0	0 1	44 8			.

Apparatus Nos. 3 and 4.—They were dried at room temperature for 3 years (June 1, 1916–May 15, 1919), and then heated to 100° for 3 periods of 10 hours each. At the end of the final period, the temperature at the very base rose to 200–250°, which caused the distillation of the salt from the bottom. However, the thermometers were still well surrounded by the caked salt. Heating and cooling curves were taken without cooling the pentoxide bulbs. Apparatus No. 3.

Heating						Cooling.					
Temp of NH₄Cl. Degrees.	Rate Degrees	Time Minutes	Temp of NH₄Cl Degrees	Rate Degrees	Time Minutes	Temp of NH₄Cl Degrees	Rate Degrees.	Time Minutes	Temp of NH₄Cl Degrees.	Rate Degrees.	Time. Minutes
170		0 0	188	+0 4	11 7	185 0		0 0	171	—1 0	10.5
174	+2 2	1 8	189	0 7	13 2	180.0	—2 4	2 1	170	0 8	11.7
178	2 5	3 2	190	0 8	14 5	175 0	2 1	4 5	169	1 2	12 5
182	2 2	5 0	191	2 0	15 0	173.0	2 5	5 3	168	2.0	13 0
184	2.0	6 0	192	1 4	15 7	172 0	1.4	6 0	167	5 0	13.2
185	3 3	6 3	193	3 3	16.0	172.5	+0 2	8.1	165	3.0	13.9
186	1 0	7 3	195	4 0	16.5	172 0	—0 4	9 5	160	4 2	15.1
187	0.5	9 3	200	3.8	17 8	...	...	...	...	...	...

The transition occurs at 186° and 172° on heating and cooling, respectively. With ordinary ammonium chloride (undried), determined at the same time, the temperatures of transition were 186° and 170°.

Apparatus No. 4.—The curves for this determination as well as for the bath temperatures and the curves for undried ammonium chloride are given in Figs. 1 and 2.

Heating.

Temp of NH_4Cl. Degrees.	Rate. Degrees	Time. Minutes.	Temp of NH_4Cl Degrees	Rate Degrees.	Time Minutes.
170		0.0	185	+1.0	12.8
174	+2.0	2.0	186	1.4	13.5
178	2.0	4.0	187	3.3	13.8
180	2.0	5.0	188	2.5	14.2
182	2.0	6.0	190	3.3	14.8
183	2.0	6.5	194	2.5	15.8
184	1.0	7.5	200	2.7	18.0
184	±0.0	11.8			

Cooling.

Temp of NH_4Cl Degrees	Rate Degrees	Time Minutes	Temp of NH_4Cl Degrees	Rate Degrees	Time Minutes.
184.0		0.0	171	+2.0	7.2
180.0	−2.7	1.5	172	+1.2	8.0
176.0	2.4	3.2	172	±0.0	9.2
172.0	2.2	5.0	171	—0.6	10.8
171.0	3.3	5.3	170	1.4	11.5
170.0	1.4	6.0	169	3.3	11.8
169.5	2.5	6.2	168	5.0	12.0
170.0	+1.0	6.7	164	4.0	13.0

Transition occurs at 184° and 172° on heating and cooling, respectively. With the undried ammonium chloride determined at the same time, the transition occurs at 184° and 173°.

Summary.

1. Ammonium chloride in the absence of water (dried 45 days at 155–165° or 3 years at room temperature with phosphorus pentoxide in a high vacuum) undergoes transition at 184.5°, the same as the undried salt.
2. In the thermal measurement of transition points in a high vacuum, confusion may result from the greater thermal effects of distillation.
3. Wegscheider's explanations of the anomalous vapor density of dried ammonium chloride by a failure to undergo transition in the absence of water are untenable in the light of these results.

New York, N. Y.

[Contribution from the Michigan College of Mines.]

THE DECOMPOSITION OF STANNOUS CHLORIDE BY WATER AND BY POTASSIUM HYDROXIDE SOLUTIONS.

By C. M. Carson.

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Introductory.

The experiments described in this paper were undertaken for the purpose of determining the composition of the precipitates formed when stannous chloride is decomposed by water. For, although the appearance of these precipitates is well known, no information concerning them is found in the literature with the exception of that contained in brief papers by Ditte,[1] published 37 years ago. Ditte states that $SnCl_2.2H_2O$, when boiled with water, forms a hydrated oxychloride $SnCl_2.SnO.6H_2O$; that this, when boiled with water to which stannous chloride is added, little by little, forms a crystalline basic salt, $2SnCl_2.3SnO.6H_2O$; and that the last named by further treatment with stannous chloride solution, yields a less basic precipitate, $SnCl_2.SnO.4H_2O$.

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[1] *Compt. rend.*, 94, 792, 864 (1882); *Ann. chim.*, [5] 27, 145 (1882).

Recently, an anhydrous basic stannous chloride has been described by Keller.[1] This material was found enclosed in a tin object brought from an Indian mound in Florida, and had approximately the composition represented by $SnCl_2.SnO$. Preliminary analysis, by Keller, of an impure specimen of it gave 67% of tin and 13.6% of chlorine, while two analyses of more carefully selected samples gave:

	%	
Sn	70.92.	73.06
Cl .	21.68	21.98
Impurities	0.26	

The present writer has prepared a crystalline basic salt with very nearly the atomic ratio given in Keller's preliminary analysis, but none with more than 17% of chlorine.

In the investigation of basic salts, the best guide is an application of the phase rule, first proposed by Miller and Kenrick.[2] Thus, if several portions of a salt which forms basic salts with water, are treated with different proportions of water at the same temperature until equilibrium ensues, 3 cases may present themselves. (1) The precipitates, in a series of mixtures, are all of the same composition, but the solutions above them are different. These precipitates are a single chemical compound. (2) The precipitates in a series are all different, but the solutions are of the same composition. These precipitates are mixtures of two compounds in varying proportions. (3) The precipitates in a series are all different and the solutions are all different. These precipitates are solid solutions.

The rules which have just been stated apply to 2 component systems. The addition of potassium hydroxide to a system made up of stannous chloride, stannous oxide and water, introduces a fourth component. Now, while variable solutions indicate a bivariant system with 3 components, they may indicate either bivariant or tervariant systems with 4 components. It is still possible to apply the rules, however, under the following conditions, as stated by Miller and Kenrick· (*a*) The ratio of water to the other components must be large; (*b*) the fourth component must not enter the precipitates; (*c*) there must be a constant ratio between the fourth component and the water.

These conditions have been partly fulfilled in the experiments to be described, for when stannous chloride is treated with potassium hydroxide, the ratio of alkali to water is kept constant and the alkali does not enter the precipitate, but the ratio of water to salt is not large.

Experimental.

The stannous chloride used in the following experiments was prepared from Baker & Adamson's C. P. salt. About 500 g. at a time was treated with tin and hydrochloric acid; the mixture was boiled gently until most of the free acid was removed and was then allowed to cool. The crystals which deposited were drained as thoroughly as possible and dried between filter papers. The product consisted of transparent, colorless crystals which dissolved in a small proportion of water, leaving no residue. The relative proportions of tin, chlorine and water in the lots of salt, prepared at different times, varied to some extent. It was found necessary, therefore, to make a batch of crystals sufficiently large for a complete series of experiments, in order that the results might be comparable.

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[1] THIS JOURNAL, 39, 2354 (1917)

[2] *J. Phys. Chem.*, 7, 259 (1903).

The first series of experiments was carried out in the following way: A weighed quantity of the salt, usually 25 g., was placed in a flask of from 100 to 1000 cc. capacity, and a measured volume of water which had been boiled vigorously for 20 minutes, to expel air, was added to it. The flask was connected to a reflux condenser, a current of nitrogen was passed through the apparatus and the mixture was boiled for 8 hours. The mixture was then filtered into a dry flask, and the precipitate and solution analyzed. The precipitates were not washed, as that would alter their compositions materially, but were dried between filter papers. Of course, the dried precipitates were contaminated with a small amount of mother liquor, but since they contained, in all cases a large amount of stannic salt, accurate knowledge of their composition would be useless. The results are given merely because the appearance of the white precipitates formed by the hydrolysis of stannous chloride is so well known.

The analysis of the solutions seemed to offer no difficulty, as they contained only stannous chloride and a small excess of hydrochloric acid. A measured volume of the mother liquor was pipetted into a weighing bottle, the weight taken and the liquid diluted in a flask. The tin was precipitated as stannous sulfide and weighed as stannic oxide. The results by this method are slightly high, but with proper precautions are consistent. The filtrate from the stannous sulfide was boiled to remove the hydrogen sulfide and was then titrated with standard sodium carbonate for the determination of total chloride.

Later experiments have shown that in the presence of even very small amounts of strong acids, stannous sulfide sometimes carries down considerable amounts of chloride, which is not removed by washing. It is possible then that the analyses of mother liquors may be inaccurate, though comparable among themselves.

The precipitates of basic chloride were ground and weighed and were first treated with 20 cc. of *N* nitric acid. The acid was next neutralized by ammonium hydroxide, acetic acid was added in excess and the volume was made up to 100 cc. with water. The precipitates were only slightly soluble in cold acids but when hydrogen sulfide was passed through the mixtures, complete transformation into tin sulfide took place. The sulfides were filtered and weighed as stannic oxide. The filtrates were boiled to remove hydrogen sulfide and were then precipitated by silver nitrate.

Determination of the tin in the basic precipitates was also made by the Lenssen-Baker method, in which the tin is titrated by iodine in conc. hydrochloric acid solution. By reduction with aluminum, the total tin was obtained, while without reduction the tin in the stannous condition was given.

In all cases where stannous chloride was boiled with water, the precipitates contained such a large amount of the stannic salt, usually about $^1/_3$ of the total, that it was impossible to decide to what extent stannous chloride is hydrolyzed. The presence of the stannic salt is probably due to the presence of about 0.5% of quadrivalent tin in the stannous chloride. The results of the first series of experiments are given in Table I.

TABLE I.

Expt.	Wt of $SnCl_2.2H_2O$ G.	Cc of water	Atomic ratio Cl : Sn in 100 cc of mother liquor	% in ppt. Tin	% in ppt. Chlorine.	Atomic ratio Sn : Cl in ppt.
1......	25	100	$\frac{0.2020}{0.1006} = 2.02$	70.99	12.00	1.76
2......	25	250	$\frac{0.0854}{0.0423} = 2.02$	72.09	10.97	1.96
3......	25	500	$\frac{0.0426}{0.0208} = 2.05$	73.16	7.88	2.76
4......	25	1000	$\frac{0.0218}{0.0106} = 2.05$	74.13	5.36	4.12
5......	15	1000	$\frac{0.0120}{0.0058} = 2.07$			
6......	10	1000	$\frac{0.0087}{0.0042} = 2.08$	75.71	4.59	4.91
7......	5	1000	$\frac{0.0043}{0.0021} = 2.08$	Partly SnO		
8....	2.5	1000	$\frac{0.0021}{0.0008} = 2.61$	Mostly SnO		
9......	1.0	1000	$\frac{0.00082}{0.00023} = 3.52$	Mostly SnO		

The precipitates in the first 6 experiments of the series were pale yellow and amorphous. Although slightly gelatinous, they filtered well. It will be seen that there is a continuous variation in the composition of the precipitates, that is, they become progressively more basic as the ratio of water to stannous chloride in the original mixture, increases. While the precipitates become more basic, the solutions become more acid, but since the precipitates are small, ranging from 0.2 to 0.5 g., the change in the composition of the solution is small.

When the weight of water in the original mixture becomes 200 times greater than the weight of salt, black crystalline stannous oxide is formed after boiling for two hours. The black crystals are mixed with some yellow precipitate, largely oxidized basic chloride. In Expts. 8 and 9, it will be observed that the solutions have become very acid, though this change might be expected in Expt. 7, where the black precipitate first appears.

The failure to distinguish basic compounds from mixtures was due to oxidation which might possibly be prevented by greater precautions, but as the desired information may be obtained by the use of potassium hydroxide solutions, the first method was abandoned. When stannous chloride is hydrolyzed by alkalies, the precipitates are not only much larger than when pure water is used, but they may also be separated from the relatively small quantity of stannic compound by decantation.

In the second series of experiments, the same ratio of stannous chloride and water was used as in the first series. The mixtures were boiled as before but, after the precipitates were filtered off, the mother liquors were preserved in corked flasks and allowed to cool overnight to 25°. These filtrates, with the exception of No. 3, deposited white amorphous precipitates only, which were less basic than those formed at the boiling point, while the mother liquors became more acid. From No. 3, in which 25 g. of salt was boiled with 500 cc. of water, a small amount of white amorphous precipitate was deposited, together with about 0.2 g. of crystals. The crystals formed hexagonal rosets of about one mm. in diameter, and adhered tenaciously to the flask in which they were deposited. The rosets are made up of thin, transparent, colorless plates. Analysis of the crystalline material gave 73.63% of tin and 16.51% of chlorine or an atomic ratio, Sn : Cl, of 1.33, which could be represented by the formula

$$3\text{SnCl}_2.5\text{SnO}.3\text{H}_2\text{O}.$$

Analysis of the amorphous precipitate, deposited along with the crystals, showed an atomic ratio of 1.93, but about 20% of the tin was in the stannic state while in the crystals the oxidation was only 0.6%. The crystals were soluble in 100 cc. of 0.3 *N* nitric acid. Washing the crystals with water, to free them from mother liquor, renders them slightly more basic, for it was shown that 0.2 g. of the substance of atomic ratio 1.33, after being washed with four 20 cc. portions of water, had an atomic ratio of 1.35.

The crystals mentioned in the preceding paragraph may be obtained in larger amounts by using stannous chloride which has been overheated during its preparation. By starting with a slightly basic salt prepared in this way, when 25 g. was boiled with 500 cc. of water for one hour, and the mixture cooled, 1.2 g. of crystals was deposited. From 0.25 to 0.5 g. of crystals was also deposited when 25 g. of the same salt was treated in the same way with

Interaction of Stannous Chloride and Potassium Hydroxide Solutions.

The next series of experiments was carried out for the purpose of determining the effect of a fixed volume of potassium hydroxide solution of a certain concentration on different weights of stannous chloride. In each experiment 100 cc. of 0.2 *N* potassium hydroxide solution was used, and the weight of the salt was varied from 3.5 to 75 g. The mixture was put in a flask which was attached to a reflux condenser, the air was displaced by a current of nitrogen and the mixture was boiled for 6 hours.

When 100 cc. of 0.2 *N* potassium hydroxide solution is added to 25 g. of stannous chloride, a pale yellow precipitate is thrown down. When the mixture has been boiled for a few minutes, however, this curdy precipitate suddenly changes to white crystals which become slightly yellow on continued boiling. The crystals settle rapidly and therefore may be washed by decantation with small amounts of water. This washing alters the composition of the crystals to some extent, but the results are probably more accurate than those which would be obtained by less direct methods.

When the volume of 0.2 *N* alkali is still 100 cc., but the weight of stannous chloride is between 3.5 and 5.5 g., the precipitate is no longer crystalline. It settles rapidly, however, and may be washed, though not so readily, as in the case of the crystalline precipitate.

After the mixtures were boiled, they were filtered, part of the filtrate was pipetted off for analysis, while the remainder was allowed to cool in a corked flask. The precipitates were washed and then dried at 80°. The analyses were conducted as before.

The results of this series of experiments are given in Table II.

TABLE II

100 cc. of 0.2 *N* Potassium Hydroxide Solution. Time of boiling, 6 hours.

Expt.	Weight of $SnCl_2.2H_2O$ G	Atomic ratio Cl:Sn in 100 cc of solution	% in crystals		Atomic ratio Sn:Cl in crystals
			Tin	Chlorine	
1	3.0	alkaline	87.6	small	SnO
2	3.5	$\frac{0.00774}{0.00403} = 1.92$	80.10	10.58	2.24
3	4.0	$\frac{0.0116}{0.0060} = 1.93$	79.95	10.93	2.18
4	5.0	$\frac{0.0158}{0.0083} = 1.91$	80.10	11.07	2.17
5	6.0	$\frac{0.0272}{0.0143} = 1.90$	73.76	15.90	1.38
6	7.0	....	73.75	16.15	1.36
7	16.0	$\frac{0.1045}{0.0550} = 1.91$	73.45	16.09	1.36
8	25.0	$\frac{0.1752}{0.0903} = 1.94$	73.31	16.52	1.32
9	30.0	....	73.41	16.55	1.30

In Expt. 2, where 3.5 g. of stannous chloride was used, there was a small amount of black stannous oxide crystals, from which the lighter yellowish precipitate was separated by decantation. It is evident, then, that the yellowish precipitate here obtained is the most basic of the basic stannous chlorides. Its composition is represented, approximately, by the formula $2SnCl_2.7Sn(OH)_2$. There is a slight variation in the composition of the precipitates in Expts. 2, 3 and 4, though this could be expected on account of the difficulty in separating the precipitates from the mother liquors. But a very striking change takes place when the amount of salt is increased to 6 g., as in Expt. 5. The precipitate becomes crystalline in character and much less basic than in Expt. 4. With increasing amounts of stannous chloride, the precipitate remains the same in appearance, but becomes somewhat less basic. When the amount of salt in the above series becomes greater than 30 g. very little precipitate is formed. This is due to the presence in the stannous chloride of a small excess of acid, which uses up most of the potassium hydroxide. To the same cause may be attributed the differences in the precipitates of Expts. 5 to 9. No attempt was made to neutralize the excess of acid in the original salt, but experiments were performed with from 40 to 75 g. of stannous chloride and 100 cc. of 0.4 *N* potassium hydroxide solution. In these the crystalline precipitates were slightly more basic than in Expt. 9.

Indications of two compounds, in addition to the oxide, are given by the results in Table II, but the variations in the precipitates from Expts. 5 to 9 were so great that they must be regarded as mixtures. This view is strengthened by two facts: first, the precipitates do not dissolve completely in dil. nitric acid, but leave small, white residues, which are due to the presence of some of the stannic compound; second, the precipitates formed when the mother liquors of experiments such as No. 9 are allowed to cool, are pure white, and dissolve in dil. nitric acid without residue. They are higher in chlorine and lower in tin than the corresponding original precipitates, and always contain less of the stannic compound.

Thus, when 50 g. of stannous chloride is boiled with 100 cc. of 0.4 *N* potassium hydroxide solution and the hot mixture is filtered, the filtrate on cooling deposits about 2 g. of the white crystals. Analysis of these crystals gave tin 72.82% and chlorine 16.93, while analysis of the original crystals, formed in the boiling liquid, gave tin 73.41% and chlorine 16.23%. The crystals deposited from the mother liquor, when 30 g. of stannous chloride was treated with 100 cc. of 0.4 *N* potassium hydroxide solution, contained 73.11% of tin and 16.76% of chlorine, while the crystals formed in the boiling liquid contained 73.93% of tin and 16.11% of chlorine.

In all cases where the original precipitate formed at the boiling point was compared with the precipitate from the cooled mother liquor by titration with iodine, it was found that the first named contained from 0.5 to 1.0% of oxidized tin, while the precipitates from the mother liquors contained only from 0.2 to 0.5%. This could only partly explain the higher chlorine content of the second crystals, even if it were assumed that the stannic compound had been completely hydrolyzed into the oxide. Other possible causes of difference are the adsorption of stannous chloride by the crystals as they separate from the mother liquor and failure to remove this by washing; or the formation along with the first crystals of some of the more basic compound by local excess of alkali, and failure to transform this into the equilibrium compound. The washing caused some change in all of the precipitates, but probably about the same amount in all.

The crystals formed when 25 g. of stannous chloride is boiled with 500 cc. of water and the mixture is allowed to cool, have already been described. They are somewhat higher in tin and lower in chlorine than the white crystals mentioned in the preceding paragraph. While in both cases the crystals are pseudo-hexagonal, in the case where pure water is used, the crystals always form rosets which are nearly spherical in shape. It might be supposed that the precipitate from the potassium hydroxide treatment contained potassium chloride which would decrease the tin and increase the chlorine content, but an analysis failed to show the presence of potassium.

An attempt was made to determine whether equilibrium had been reached in the preceding experiments, by utilizing the reverse reaction. Five g. of stannous oxide was boiled with 25 cc of 1.96 *N* hydrochloric acid for 5 hours. The mixture was filtered and the crystals and mother liquor were analyzed. It was found that 100 cc. of the mother liquor contained 1.614 gram-atoms of chlorine and 0.827 of tin, a ratio of 1.95; while the crystalline precipitate contained 73.91% of tin and 16.13% of chlorine. That is, the precipitate is very nearly of the same composition as that of Expt. 7, Table II.

The solutions and precipitates obtained in this way are of the same character as those given by the treatment of stannous chloride with potassium hydroxide solution. But the experiment did not give definite proof that equilibrium had been established, since the mother liquor was much more concentrated than when potassium hydroxide was used.

Summary.

It seems definitely proved that a compound $2SnCl_2.7Sn(OH)_2$ is the most basic of the basic stannous chlorides; that a slightly variable crystalline material, of approximately the formula $3SnCl_2.5SnO.3H_2O$, is the precipitate commonly formed by the action of boiling solutions of potassium hydroxide on an excess of stannous chloride; and that there is no

compound of intermediate composition. Whether any basic compound lies between $3SnCl_4.5SnO.3H_2O$ and the normal salt was not determined. The precipitates usually formed by the interaction of stannous chloride and water contain such a large proportion of stannic compound that the analyses are of no value in ascertaining the composition of the basic stannous chlorides.

In conclusion, I wish to express my indebtedness to Prof. Lash Miller, of the University of Toronto, who suggested this problem some years ago, and gave me considerable help with it.

HOUGHTON, MICH

[CONTRIBUTION FROM THE KENT CHEMICAL LABORATORY OF THE UNIVERSITY OF CHICAGO.]

THE EFFECTS OF ACIDS AND BASES ON THE SURFACE ENERGY RELATIONS OF β,β-DICHLOROETHYLSULFIDE ("MUSTARD GAS").[1]

BY WILLIAM D HARKINS AND D T EWING

Received September 20, 1919.

This investigation was undertaken in order to determine the relative efficiencies of various substances in the emulsification of β,β-dichloroethylsulfide in water, and with the idea that the results obtained would be of importance in connection with a study of its physiological action. The importance of the effects of acids and bases on interfacial tension has been pointed out by Haber and Klemenciewicz.[2] An active part of a muscle is always electrically negative toward the part at rest, and the active muscle is acid in reaction while the resting muscle is slightly alkaline. An acid reaction always causes the phase which corresponds with the water at the water-benzene interface, to become negative, and in the muscle this aqueous phase is represented by the sarcoplasma in which the sarcostyles are imbedded. An interface of this nature acts as a hydrogen electrode, and it would seem probable that in addition to the change of electromotive force at the phase boundary, there should also be a change of surface tension near the neutral point with reference to the change from an acid to a basic reaction. The investigation which is commonly cited to show that laboratory experiments on simple two-phase systems seem to confirm this point of view, is that of von Lerch,[3] who, while working under Nernst's direction, found that the presence of sodium hydroxide at a concentration of 0.027 *N* in the aqueous phase, caused an extremely great lowering of the interfacial tension at the water-benzene phase boundary, a lowering amounting to 36%. At the request of Professor Haber the investigation was repeated by Harkins,[1] who found the results of von Lerch to be erroneous, and that at such concentrations bases do not lower the interfacial tension of the benzene-water system at all. The apparent lowering obtained by von Lerch was apparently due to the effects of the base upon the glass, which lowers the height of the liquid in a capillary tube when there is no lowering of surface tension caused by the base alone.

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[1] An investigation undertaken at the request of the National Research Council and suggested to them by Lieutenant Colonel A. B. Lamb and Major R. E. Wilson.

[2] *Z. physik. Chem.*, 76, 385–431 (1909)

[3] [illegible]

Benzene and saturated paraffin hydrocarbons are chemically too indifferent toward bases to give the surface tension lowering described in the last paragraph. Chloroform,[2] to some extent, and β,β-dichloroethylsulfide, much more markedly, give the lowering of interfacial tension toward water, when bases, but not when acids are added, and the magnitude of the actual effect is much greater than the fictitious one found by von Lerch. Thus 0.1 *N* sodium hydroxide solution reduces the interfacial tension at the water-dichloroethylsulfide phase-boundary by 55%.

The surface tension at 20° between β,β-dichloroethylsulfide and water is 28.36 dynes per cm., or about 5 dynes less than that between benzene and water. The surface tension of this liquid toward its vapor is 42.82 dynes per cm., which is 14 dynes higher than that of benzene. One of the most important characteristics of a liquid in this connection is the amount of work done when one square centimeter of the surface of the liquid approaches one square centimeter of a water surface. This value is 87.3 ergs in the case of β,β-dichloroethylsulfide, which indicates that this liquid, while only very slightly soluble in water, has a high attraction for it, although the magnitude of the work done is slightly less than that found for an alcohol. The following table (Table I) gives values for this work for a number of classes of organic substances:

TABLE I

Liquid	Work done ($-\Delta\gamma$) by the attractive forces between water and the liquid per sq. cm. of each.
Sulfur compounds	$-\Delta\gamma$
β,β-Dichloroethylsulfide	87.26
Mercaptan	68.50
Carbon disulfide	55.82
Octane	43.76
Benzene	66.63
Alcohols	93.0
Organic acids	95.0
Monochloroacetone	101.00
Dichloroacetone	90.28
Chloroform	67.30
Methylene chloride	71.00

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[1] Harkins, Davies, and Clark, THIS JOURNAL, 39, 548–9 (1917).

[2] N. D. Thatcher in this laboratory has obtained results which show that the surface tension at the interface water-chloropicrin is not lowered by either HCl or NaOH,

According to the theory of Harkins,[1] the interfacial tension at a phase-boundary is lowered by any substance which makes the transition between the two phases more gradual with respect to the intermolecular electromagnetic fields.[2] A large number of substances might have been found which would have done this, but the only ones investigated were corn oil, Twitchell's solution, and turkey-red oil. All of these proved extremely effective in lowering the interfacial tension at the water-dichloroethylsulfide interface. The effectiveness of both the corn oil and the turkey-red oil were considerably increased by making the solutions alkaline with sodium carbonate at 0.1 *N* concentration, but this did not seem to be the case with Twitchell's solution. All of these substances proved to be remarkably effective as emulsifying agents, especially turkey-red oil, together with sodium carbonate.

Table II gives the results of the surface-tension determinations, which were made by the drop-weight method, using the proper precautions as determined by Harkins and Brown.[3] The radius of the tip used was 0.24995 cm. for all of the interfacial work, except when a 0.1% solution of turkey-red oil was used in the absence of sodium hydroxide, when the radius was 0.275 cm. For the dichloroethylsulfide alone a tip of 0.27441 cm. radius was used. The density of this latter liquid was 1.2732 g. per cc. In all of the experiments the aqueous solution was dropped upward through this liquid without allowing time for mixing.

TABLE II

The Surface Tension between β,β Dichloroethylsulfide and Various Aqueous Solutions in Dynes per Cm.

Substance	Vol. of 1 drop in cc.	Density of substance	r/a	Surface tension.
Vapor	0.03555		1.04	42.82
Water	0.1062	0.9982	0.595	28.36
0.1 *N* HCl	0.1090	1.00011	0.5385	28.90
0.1 *N* NaOH	0.04612	1.0032	0.8066	12.78
0.1 *N* Na_2CO_3	0.0695	1.0025	0.6635	18.82
1% Soln. turkey-red oil	0.0567	1.0000	0.607	14.47
1% Soln. turkey-red oil in 0.1 *N* Na_2CO_3	0.02977	1.0035	1.00	8.35
			$r/v^{1/3}$	
1% Twitchell's Soln.	0.04384	0.99924	0.7088	12.32
1% Twitchell's Soln. in 0.1 *N* Na_2CO_3	0.04663	1.00311	0.6944	12.89
1% Corn oil Soln.	0.4577	0.9984	0.698	12.94
1% Corn oil Soln. in 0.1 *N* Na_2CO_3	0.03936	1.0036	0.735	10.91

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[1] Harkins, Brown, Davies and Clark, THIS JOURNAL, **39**, 354–64, 541–96 (1917); Harkins and King, *Ibid.*, **41**, 970–92 (1919), especially pp. 480–3.

[2] The theory of Langmuir, which does not specifically refer to interfaces, leads to the same conclusions. See *Met. Chem. Eng.*, **15**, 468 (1916); *Proc. Nat. Acad. Sci.* **3**, 251–7 (1917); THIS JOURNAL, **39**, 1848–1906 (1917); see also Frankel, *Phil. Mag.*, **33**, 297 (1917) and especially Hardy, *Proc. Royal Soc.*, **86B**, 634 (1911–12).

[3] THIS JOURNAL, **41**, 499–524 (1919).

The values for r/a and $r/v^{1/3}$ indicate the shape of the drop. A discussion of this subject will be found in the paper of Harkins and Brown.

Table III gives data for the surface tension of a number of organic liquids prepared by Professor Huston of the Michigan State Agricultural College. Unfortunately, the two temperatures at which the measurements were made are not sufficiently far apart to give good values of the temperature coefficients. The tip used had a radius of 0.27441 cm.

TABLE III

The Surface Tension of Some Organic Liquids

Substance	Temp	Wt of 1 drop in g	Density	$r/v^{1/3}$.	Surface tension. Dynes per cm.
Diphenyl propane	20°	0 03920	0 9998	0 808	37.15
$(C_6H_5)_2CHCH_2CH_3$	25°	0 03865	0 9962	0 801	36.64
1,1-Diphenyl ethane	20°	0 03975	1 0039	0 807	37 67
	25°	0 03925	0 9998	0 808	37 20
Diphenyl methane	26°	0 03963	1 0044	0 806	37.56
Ditolyl methane	20°	0 03745	0 9800	0 816	35 51
$(CH_3C_6H_4)_2CH_2$	25°	0 03670	0 9777	0 821	34 80
Propyl benzene or phenyl propane	20°	0 03396	1 0216	0 854	32 22
	25°	0 03299	1 0166	0 863	31 30

These liquids have a high surface tension for substances which contain carbon and hydrogen alone. It is apparent that the surface tension increases with the number of phenyl groups, with the degree of unsaturation, and with the decrease in the length of the paraffin chain. This is illustrated by the result of Jaeger, who obtains a much higher surface tension still for triphenyl methane, 44 7 dynes per cm. at 20°. Benzene has a much lower surface tension, which at 20° amounts to only 28 9 dynes per cm. The tolyl group increases the surface tension much less than the phenyl group. Former studies in this laboratory have also shown that the methyl group lessens the effect of phenyl groups, since the electromagnetic stray field around the methyl groups is much less, and this causes them to be oriented into the surface.

CHICAGO, ILLINOIS.

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF COLUMBIA UNIVERSITY. No. 328.]

CONTRASTING EFFECTS OF CHLORIDES AND SULFATES ON THE HYDROGEN ION CONCENTRATION OF ACID SOLUTIONS.

BY ARTHUR W THOMAS AND MABEL E BALDWIN.

Received September 23, 1919.

In the process of chrome tanning the practical tanner has discovered that by addition of neutral salts it is possible to use more basic chrome liquors. The added salt prevents the precipitation of hydrous chromic oxide. Wilson and Kern[1] believe that this phenomenon is due to increase in the hydrogen ion concentration caused by removal of water from the solvent to hydrate ions of the added salts.

Since Wilson and Kern did not actually measure the hydrogen ion concentration of these solutions, the authors of this paper took up the problem with the result that a striking contrast in the effect of chlorides, and sulfates and magnesium salts on solutions of hydrochloric and sulfuric acids has been noted.

In our first experiment the effect of sodium chloride, ammonium chloride, sodium sulfate, ammonium sulfate and magnesium sulfate upon the hydrogen ion concentration of a stock chrome liquor,[2] diluted to contain 13.86 g. of chromic oxide per liter, was determined. These figures are given in Table I and Fig. 1.

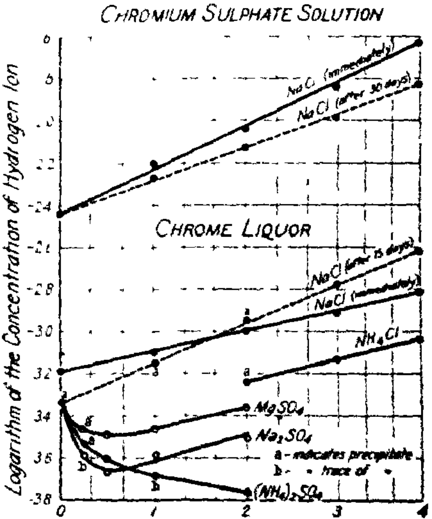

Fig. 1.

It will be noted that equilibrium in hydrogen ion concentration is not reached immediately after dilution of a concentrated chrome liquor by water or by salt solution. This effect is shown in Table II and Fig. 2. This slow increase in hydrogen ion concentration in solutions of chromic salts has been long known and has been shown to be due to the trans-

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[1] *J. Am. Leather Chem. Assoc.*, 12, 445 (1917).

[2] This stock chrome liquor analyzed by and furnished to us by Mr. John Arthur Wilson, of Milwaukee, showed: Cr_2O_3, 14.3%; Fe_2O_3, 1.9%; Al_2O_3, 0.2%; SO_3, 23.5%; NaCl, 0.4%; glucose, none; sp. g., 1.628 at 80° F.

TABLE I

Effect of Neutral Salts upon the Concentration of Hydrogen Ion of Chrome Liquor.

Sodium Chloride

Concentration of salt Molar strength.	Log C_{H^+} immediately	Log C_{H^+} after 15 days
0	—3.19	—3.33
1	—3.10	—3.14
2	—3.00	—2.95
3	—2.92	—2.78
4	—2.81	—2.62

Ammonium Chloride.

Concentration of salt Molar strength	Log C_{H^+} after 30 days
0	—3.33
2	—3.24
3	—3.14
4	—3.04
5	—2.95

Sodium Sulfate

Concentration of salt Molar strength	Log C_{H^+} after 30 days
0	—3.33
0.25	—3.59
0.5	—3.67
1.0	—3.58
2.0	—3.51

Ammonium Sulfate

Concentration of salt Molar strength	Log C_{H^+} after 30 days
0	—3.33
0.25	—3.54
0.5	—3.60
1.0	—3.68
2.0	—3.77

Magnesium Sulfate

Concentration of salt Molar strength	Log C_{H^+} after 30 days
0	—3.33
0.25	—3.47
0.5	—3.49
1.0	—3.46
2.0	—3.36

Effect of Sodium Chloride on Chromium Sulfate Solution

Concentration of salt Molar strength	Log C_{H^+} immediately	Log C_{H^+} after 30 days
0	—2.43	—2.43
1	—2.22	—2.28
2	—2.04	—2.13
3	—1.84	—1.98
4	—1.63	—1.83

formation of the acido chromic salt into a more largely hydrolyzed hexaaquo salt.[1]

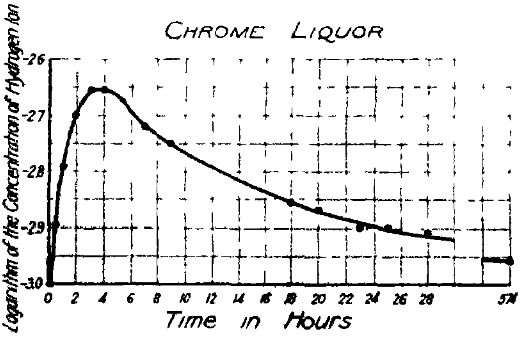

Fig. 1.

The effect noted above is not due entirely to the added salt, as can be observed in Table I and Fig. 1, where the log C_{H^+} of the chrome liquor with no added salt was observed to be —3.19 immediately after dilution and —3.33 fifteen days after dilution.

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[1] Bjerrum, *Z physik Chem*, 89, 336 and 581 (1907), also *Kgl. D. Vid. Selsk.* [illegible]

TABLE II.

Influence of Time upon the Hydrogen Ion Concentration of a Chrome Liquor after Addition of Sodium Chloride and Dilution.

Time, min.	Log C_{H^+}	Time, hrs	Log C_{H^+}
10	-3.00	3	-2.66
20	-2.94	4	-2.66
30	-2.89	7	-2.72
40	-2.85	9	-2.75
50	-2.82	18	-2.86
60	-2.79	20	-2.87
70	-2.77	23	-2.90
80	-2.75	25	-2.90
90	-2.73	28	-2.91
100	-2.72	34	-2.92
110	-2.70	46	-2.96
120	-2.70	57	-2.96
130	-2.69	15 days	-2.96
140	-2.69		
150	-2.68		
160	-2.67		
170	-2.66		

The effect of sodium chloride upon a solution of pure chromium sulfate of chromium content equal to that of the chrome liquor is also shown in Table II.

Since a rather complicated system is obtained by the mixture of solutions of chlorides with chromium sulfate it was deemed advisable to compare the effect of chlorides upon pure chromium chloride solutions.

A concentrated solution of the green modification of chromium chloride was made up for use as a stock solution, and this solution was mixed with solutions of the chlorides and then made up to volume to contain chromium chloride equivalent to 13.77 g. of Cr_2O_3 per liter in each case and the added chloride at the concentrations given.

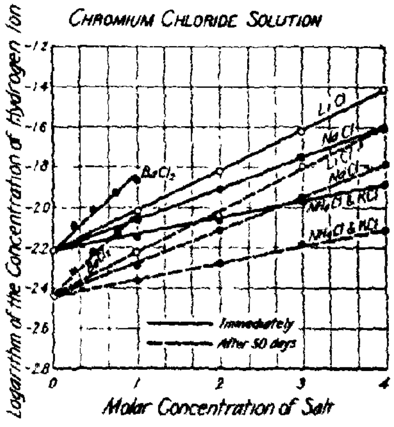

Fig. 3.

The results of these experiments are shown in Table III and Fig. 3.

It is evident that substantially the same phenomena occur here as in the mixture of chlorides and chromium sulfate.

It was then considered expedient to test the

Table III.

Effect of Chlorides upon the Concentration of Hydrogen Ion of Chromium Chloride Solution.

Concentration of salt Molar strength.	Log $C_{H}+$ immediately.	Log $C_{H}+$ after 50 days
	Sodium Chloride.	
0	—2.22	—2.43
1	—2.06	—2.24
2	—1.91	—2.11
3	—1.75	—1.95
4	—1.59	—1.79
	Potassium Chloride.	
0	—2.22	—2.43
1	—2.15	—2.36
2	—2.06	—2.28
3	—1.97	—2.19
4	—1.88	—2.12
	Ammonium Chloride	
0	—2.22	—2.43
1	—2.14	—2.36
2	—2.07	—2.30
3	—1.97	—2.19
4	—1.88	—2.14
	Lithium Chloride	
0	—2.22	—2.43
1	—2.01	—2.22
2	—1.82	—2.04
3	—1.62	—1.80
4	—1.41	—1.60
	Barium Chloride.	
0	—2.22	—2.43
0.25	—2.09	—2.32
0.5	—2.02	—2.23
0.75	—1.93	—2.13
1.0	—1.86	—2.05

Table IV.

Effect of Salts upon the Concentration of Hydrogen Ion of 0.0005 *N* Sulfuric Acid

Concentration of salt. Molar strength.	Log $C_{H}+$.	Concentration of salt. Molar strength	Log $C_{H}+$.
Sodium Chloride.		Ammonium Chloride.	
0	—3.50	0	—3.50
1	—3.29	2	—3.27
2	—3.10	3	—3.14
3	—2.92	4	—3.00
4	—2.71	5	—2.88
Sodium Sulfate.		Ammonium Sulfate.	
0	—3.50	0	—3.50
0.25	—4.37	0.25	—4.00
0.5	—5.10	0.5	—4.00
1.0	—6.05	1.0	—4.00
2.0	—6.92	2.0	—4.00

sulfates on solutions of sulfuric and hydrochloric acids of such concentrations as to give approximately the same hydrogen ion concentrations as the chromium sulfate and chloride. The concentrations were found to be 0.0005 N sulfuric acid and 0.004 N hydrochloric acid. The results of addition of salts to these acids are shown in Tables IV and V, and Figs. 4 and 5.

The similarity in the contrasting effects of sulfates and chlorides on simple acid solutions of hydrogen ion concentrations equal to those of the chromium sulfate and chloride solutions demonstrates that this phenomenon is not pertinent to solutions of chromium salts alone.

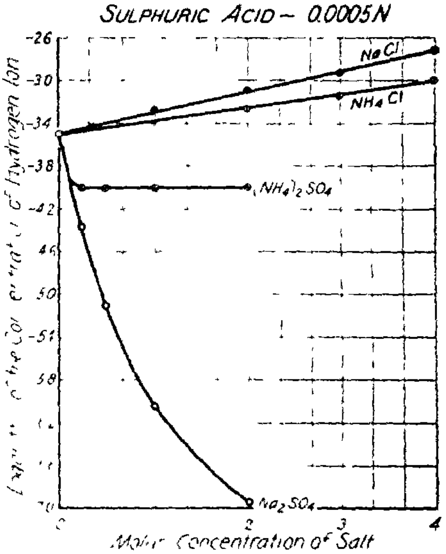

Fig. 4.

Since the effect is general with acid solutions it was considered of importance to make a series of determinations upon acids of 0.1 N (equivalent) concentration. Due to the difference in behavior of magnesium sulfate from the other sulfates, magnesium chloride was included with the salts previously tried.

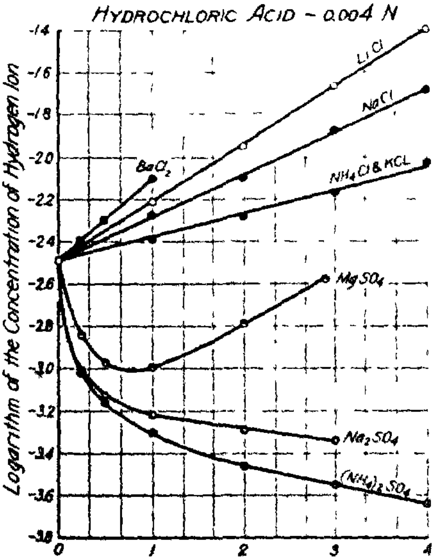

Fig. 5.

In all cases, a solution of acid was mixed with a solution of a salt and diluted to 100 cc. The concentration of this solution of the mixture was always 0.1 N (equivalent) with respect to the acid and that particular concentration of the salt whose effect upon the hydrogen ion concentration was to be studied. The hydrogen ion concentrations were measured two days after the solutions were made up

TABLE V.

Effect of Chlorides upon the Concentration of Hydrogen Ion of 0.004 *N* Hydrochloric Acid.

Concentration of salt. Molar strength.	Log C_{H^+}	Concentration of salt Molar strength	Log C_{H^+}.
Sodium Chloride		Potassium Chloride.	
0	−2.49	0	−2.49
1	−2.27	1	−2.39
2	−2.10	2	−2.28
3	−1.88	3	−2.17
4	−1.60	4	−2.03
Ammonium Chloride		Lithium Chloride.	
0	−2.49	0	−2.49
1	−2.37	1	−2.21
2	−2.27	2	−1.95
3	−2.18	3	−1.67
4	−2.03	4	−1.40
Barium Chloride		Sodium Sulfate	
0	−2.49	0	−2.49
0.25	−2.40	0.25	−3.01
0.5	−2.30	0.5	−3.13
1.0	−2.10	1.0	−3.22
		2.0	−3.29
		3.0	−3.34
Ammonium Sulfate		Magnesium Sulfate.	
0	−2.49	0	−2.49
0.25	−3.02	0.25	−2.84
0.5	−3.16	0.5	−2.97
1.0	−3.30	1.0	−2.99
2.0	−3.46	2.0	−2.79
3.0	−3.55	3.0	−2.58
4.0	−3.64		

Tables VI and VII, and Figs. 6 and 7 show the results obtained.

It may be noted here that the relative effect of ammonium sulfate and sodium sulfate on 0.1 *N* sulfuric acid differs from that on 0.0005 *N* sulfuric acid as shown in Fig. 4. In the case of the 0.0005 *N* acid, ammonium sulfate decreases the hydrogen ion concentration at 0.25 molar concentration of the salt and no further decrease is noted for higher concentrations. This is probably due to the slight acid reaction of ammonium sulfate which is noticeable in such dilute acid as 0.0005 *N*, but not in the presence of 0.1 *N* sulfuric acid.

The effect of chlorides in increasing the hydrogen ion concentration of hydrochloric acid solutions is not new. This has previously been shown by Poma,[1] Harned[2] and by Fales and Nelson.[3] Arrhenius[4] found that

[1] *Z. physik. Chem.*, 88, 671 (1914).

[2] THIS JOURNAL, 37, 2460 (1915).

[3] *Ibid.*, 37, 2769 (1915)

[4] *Z. physik. Chem.*, 31, 197 (1899).

the hydrogen ion activities of acetic and of hydrochloric acids were increased by neutral salts which he thought was due to the salts increasing the dissociation of the acids, but in the light of recent work on hydration of ions in aqueous solutions, a more plausible explanation is offered,[1] namely, that the volume of solvent appears to decrease.

When the chlorides are arranged in order of their ability to increase the hydrogen ion activity, the following series is obtained: $MgCl_2 > BaCl_2 > LiCl > NaCl > NH_4Cl = KCl$ which, with the exception of magnesium and of barium, is in inverse order to a series of these cations arranged in order of their equivalent conductivities.

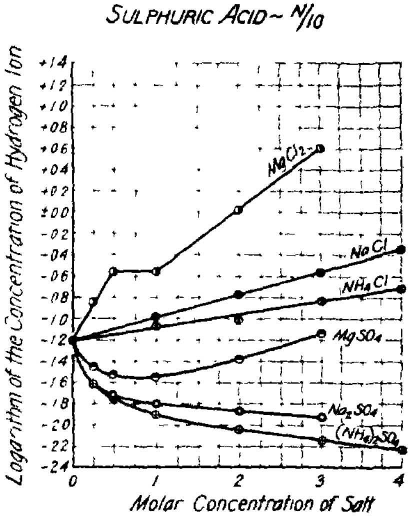

Fig. 6

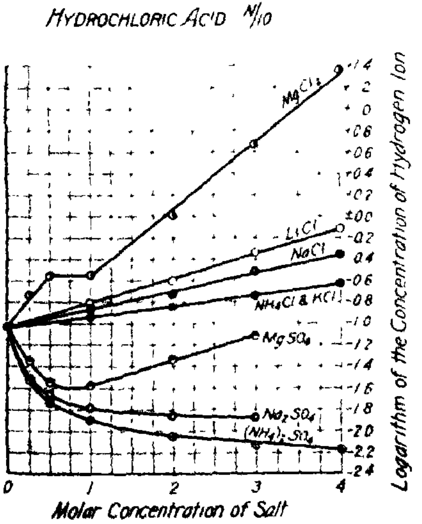

Fig. 7.

In the above series the salts are arranged in order of the increasing hydration (*i. e.*, number of molecules of water combined with the ions at infinite dilution) of their cations, K^+, 9.6; NH_4^+, 10.7; Na^+, 16.9; Li^+, 24.0,[2] Ba^{++}, relatively higher;[3] Mg^{++}, higher than Ba^{++}.[4]

Poma[5] found that chlorides increased the hydrogen ion concentration of hydrochloric acid solutions in the following order: $MgCl_2 > CaCl_2 > LiCl > KCl > RbCl$.

The noteworthy feature of this paper is the contrast shown between the decreasing hydrogen

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[1] Poma, *Loc. cit.* Poma and Patroni, *Z. physik. Chem.*, **87**, 197 (1914); Harned, *Loc. cit.*; Smith, THIS JOURNAL, **37**, 722 (1915).

[2] Smith, *Loc cit*

[3] Washburn, *Tech Quart.*, **21**, 360 (1908).

[4] Jones, *Carnegie Inst. Pub.*, **60** (1907).

[5] *Loc cit.*

TABLE VI

Effect of Salts upon the Concentration of Hydrogen Ion of 0.1 *N* Sulfuric Acid

Concentration of salt Molar strength	Log C_{H^+}	Concentration of salt Molar strength.	Log C_{H^+}.
Sodium Chloride		Ammonium Chloride	
0	−1.21	0	−1.21
1	−0.99	1	−1.08
2	−0.78	2	−0.98
3	−0.57	3	−0.84
4	−0.36	4	−0.72
Magnesium Chloride		Sodium Sulfate	
0	−1.21	0	−1.21
0.25	−0.84	0.25	−1.60
0.5	−0.56	0.5	−1.72
1.0	−0.56	1.0	−1.80
2.0	+0.03	2.0	−1.88
3.0	+0.60	3	−1.92
Ammonium Sulfate		Magnesium Sulfate	
0	−1.21	0	−1.21
0.25	−1.61	0.25	−1.46
0.5	−1.76	0.5	−1.52
1.0	−1.90	1.0	−1.53
2.0	−2.04	2.0	−1.39
3.0	−2.15	3.0	−1.15
4.0	−2.24		

ion effect of sulfates and the increasing effect of chlorides on acid solutions, and the interesting similarity of the distribution of the plots between the sulfuric acid salt systems and the hydrochloric acid salt systems. We are not prepared to offer an explanation for the above but are in agreement with the statement made by Harned[1] that "when more complete thermodynamic data are available, the calculation of equilibria in concentrated solutions will be rendered possible," and that if, as he has indicated "the thermodynamic degrees of dissociation or activities are a simple function of the ionic hydration values, the whole behavior of a concentrated solution of an electrolyte will become explicable."

The peculiar effect of magnesium salts is interesting, especially in that the concentrations for bends in the curves are in each case between 0.5 and 1 molar. We have tried to find an explanation for these peculiarities in Jones' "Hydrates in Aqueous Solutions."[2] Jones states, "Magnesium sulfate, like all the other sulfates studied, gives abnormal results. It appears to form no hydrates in aqueous solution, notwithstanding the fact that it crystallized with seven molecules of water of crystallization. It is almost certain that this substance has considerable hydrating power, but this is masked in our results by the large amount of polymerization which the sulfates undergo."

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[1] THIS JOURNAL, 40, 1481 (1918).

[2] *Carnegie Inst. Pub* 60 (1907).

TABLE VII.

Effect of Salts upon the Concentration of Hydrogen Ion of 0.1 *N* Hydrochloric Acid.

Concentration of salt. Molar strength.	Log $C_{H}+$	Concentration of salt Molar strength	Log $C_{H}+$.
Sodium Chloride.		Potassium Chloride.	
0	−1.038	0	−1.038
1	−0.88	1	−0.95
2	−0.72	2	−0.85
3	−0.52	3	−0.75
4	−0.36	4	−0.63
Ammonium Chloride.		Lithium Chloride	
0	−1.038	0	−1.038
1	−0.94	1	−0.81
2	−0.87	2	−0.60
3	−0.75	3	−0.35
4	−0.65	4	−0.12
Barium Chloride.		Magnesium Chloride.	
0	−1.038	0	−1.038
0.25	−0.96	0.25	−0.73
0.5	−0.88	0.5	−0.55
0.75	−0.80	1.0	−0.55
1.0	−0.71	2.0	+0.005
		3.0	+0.68
		4.0	+1.37
Sodium Sulfate.		Ammonium Sulfate.	
0	−1.038	0	−1.038
0.25	−1.51	0.25	−1.52
0.5	−1.65	0.5	−1.72
1.0	−1.79	1.0	−1.90
2.0	−1.86	2.0	−2.05
3.0	−1.89	3.0	−2.14
		4.0	−2.18
Magnesium Sulfate.			
0	−1.038		
0.25	−1.36		
0.5	−1.45		
1.0	−1.47		
2.0	−1.34		
3.0	−1.12		

The curve of freezing-point depression of magnesium sulfate plotted against concentration shows a depression to about 0.5 molar from which point the depression decreases for higher concentrations. In this respect there is a slight similarity to its decreasing effect on hydrogen ion concentration to 0.5 to 1 molar, beyond which it increases it. Magnesium chloride, however, gave a similar effect on freezing-point depression, although not so pronounced as magnesium sulfate.

We do not believe that the figures for hydrogen ion concentrations in the presence of salts (except in dilute solutions) given in this paper, are the true values. They should be termed apparent concentrations of hydrogen ion as determined by the method in general use at this date.

Apparatus and Method.

For the determination of the hydrogen ion concentration, a Wolff 15,000 ohm bridge with a galvanometer to determine the null point was used. As hydrogen electrode, a No. 16 Brown and Sharpe gage platinum wire (platinized) fused in a glass tube inserted in the Clark[1] cell was used. The calomel element contained 3.5 molar potassium chloride solution saturated with calomel and was the same design as that described by Fales and Vosburgh.[2] The e. m. f. was determined by means of a Weston cell that had been checked by the Bureau of Standards. The hydrogen contained in a tank under pressure, was carefully washed through saturated mercuric chloride solution, alkaline permanganate, alkaline pyrogallol and a tower of cotton fibers. The measurements were made at room temperatures which varied between 22° and 26°, the proper corrections being made. No correction for barometric pressure was made since this correction is so small.[3] No attempt was made to calculate and correct for the solution contact potential because we know of no satisfactory method of doing so, especially where solutions containing divalent ions are concerned. It is emphasized, however, that the differences in effects reported in this paper cannot be attributed to solution contact potential. This point was demonstrated by Harned, and Fales and Vosburgh[4] proved that there is no contact potential at 25° between a saturated solution of potassium chloride (4.1 *M*) and hydrochloric acid solutions ranging in concentrations between 0.1 molar and 1.0 molar.

The salt bridge between the hydrogen and calomel elements used in our measurements was a saturated solution of potassium chloride.

We are greatly indebted to the Messrs. A. F. Gallun and Sons Company, of Milwaukee, for grants in aid of this investigation, and to the editor of THIS JOURNAL for his helpful criticism of the manuscript.

NEW YORK, N. Y.

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[1] Clark, *J. Biol. Chem.*, 23, 475 (1915).

[2] THIS JOURNAL, 40, 129 (1918).

[3] See Harned, *Loc. cit.*

[4] *Loc. cit.*

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THROOP COLLEGE OF TECHNOLOGY. No. 5.]

THE VAPOR PRESSURES AND FREE ENERGIES OF THE HYDROGEN HALIDES IN AQUEOUS SOLUTION; THE FREE ENERGY OF FORMATION OF HYDROGEN CHLORIDE.

BY STUART J. BATES AND H. DARWIN KIRSCHMAN.[1]

Received September 22, 1919.

Contents: 1. Purpose of the Investigation. 2. Previous Determinations. 3. Description of Method and Apparatus. 4. Preliminary Experiments. 5. Method of Computing the Results. 6. Experimental Data and Computed Vapor Pressures. 7. Comparison with Electromotive-Force Data. 8. The Free Energy of Formation of Hydrogen Chloride and of the Hydrogen Halides in Solution. 9. Summary.

1. Purpose of the Investigation.

The free energy of formation of the hydrogen halides at ordinary temperatures may be calculated readily by the aid of electromotive force data and of vapor pressure measurements. Thus, from the electromotive force of the cell H_2 (1 atm.), HCl (c molal), Cl_2 (1 atm.), may be calculated the free energy of 1 HCl in c molal solution. By adding to this the free-energy increase attending the compression of 1 HCl from the pressure at which hydrogen chloride is in equilibrium with its c molal solution to a pressure of one atmosphere, the free energy of formation of hydrogen chloride is obtained.

The necessary electromotive force data, in the case of hydrogen chloride, have been determined with a considerable degree of accuracy, but, as pointed out by Ellis,[2] the existing data for the partial pressures of hydrogen chloride above its aqueous solutions at 25° are not at all consistent. This investigation was undertaken with the object of securing the necessary vapor pressure data.

In addition the vapor pressures at 25° of hydrogen bromide and of hydrogen iodide above their aqueous solutions were determined. The previous data[3] for these acids are very fragmentary, none of it is at 25°. The absence of the necessary electromotive force data makes impossible the computation of the free energies of formation of these halides by the method employed for hydrogen chloride, fortunately it has been possible to calculate these values from other data.

2. Previous Determinations.

A comparison of the values determined by Gahl[4] at 25° and by Dolezalek[5] at 30° for the partial pressures of hydrogen chloride above its aqueous solutions indicates inaccuracy in the methods of one or of both of these investigators. Thus from Dolezalek's results Linhart[1] calculated the vapor pressure of a solution containing 6.75 mols of hydrogen chloride per 1000 g. of water to be 0.27 mm. at 25°, while Gahl determined the vapor pressure of a solution of this concentration to be but 0.08 mm.

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[1] DuPont Scholar, 1918-19, Throop College of Technology.

[2] THIS JOURNAL, **38**, 737 (1916).

[3] Bodenstein and Geiger, *Z. physik. Chem.*, **49**, 70 (1904); Stegmuller, *Z. Elektrochem.*, **16**, 85 (1910).

[4] *Z. physik. Chem.*, **33**, 178 (1900).

[5] *Ibid.*, **26**, 334 (1898).

Dolezalek's method consisted in passing a mixture of hydrogen and oxygen generated by the electrolysis of a potassium hydroxide solution through saturators filled with the hydrochloric acid, and then, through an apparatus for absorbing the hydrogen chloride. The volume of the gases passed was calculated from the difference in weight of the generating apparatus before and after a run. The hydrogen chloride was absorbed in standard potassium hydroxide solution and its amount determined by titrating back with acid. Eight to fifteen liters of gas were passed in from 5 to 8 hrs. In this way vapor pressures at 30° of hydrogen chloride above its aqueous solutions from 5 to 10 N were determined.

Gahl investigated the vapor pressures at 25° of hydrogen chloride in equilibrium with its solutions from 1 to 6 N. He passed a mixture of hydrogen and oxygen generated by the electrolytic decomposition of a potassium hydroxide solution through saturators filled with hydrochloric acid and then through a conductivity cell containing about one cc. of water. The volume of gases passed was calculated from the quantity of electricity used in decomposing the potassium hydroxide solution. The gases were bubbled through saturators consisting of spiral tubes about one cm. in diameter. The amount of hydrogen chloride taken up by the water in the cell was determined by measuring the conductivity of the resulting solution.

3. Description of Method and Apparatus.

The method employed in this investigation was to determine the hydrogen halide contained in a given quantity of air[2] in equilibrium with its aqueous solution and compare this with the amount of water vapor which the same air contained when in equilibrium with pure water at the same temperature. From a knowledge of the vapor pressure of water at the temperature of the experiment, the vapor pressure of the halide may then be computed.

The air was first passed through a preliminary saturating apparatus which consisted of a series of 3 Emmerling tubes containing glass beads and partially filled with a solution of acid of the same concentration as that used in the saturator. From these tubes the air was led into the saturator; this was of the type designed by Berkeley and Hartley[3] with the modifications made by Washburn and his associates.[1] The chief advantage of this type of saturator is that the air does not bubble through the solution, but passes over it and along the walls of the vessel which are being continually wet with the solution. In this way more complete saturation is obtained than in the more commonly employed air-bubbling method, and danger of carrying spray over into the absorber is greatly reduced. Indeed, as was shown in this investigation, it is made entirely negligible. The total length of path over which the air travelled in passing through the saturator was about 140 cm. Each of the first 5 limbs of the saturator was about $^1/_3$ filled by placing in it 30 cc. of acid solution while the last limb contained only 10 cc.

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[1] This Journal, 39, 2601 (1917)

[2] Nitrogen was employed in the case of hydrogen iodide.

[3] *Proc. Roy. Soc. London*, 77, 156 (1906)

The hydrogen halide was then absorbed from the saturated air by passing the latter over a dil. sodium hydroxide solution contained in a small two-limbed absorber. This was similar in construction to the saturator and contained about 10 cc. of the solution in each limb. The solutions employed contained no detectable trace of halides; their concentrations varied from 0.1 to 0.5 *N*, depending upon the amount of halide which was to be absorbed.

After the absorption of the hydrogen halide gas, the air, already almost saturated with water vapor, was completely saturated by passing it through a saturator of the same type and size as that used for the halide saturation. The amount of water contained in this air was determined by absorbing it in a series of 4 U-tubes, the first of which contained calcium chloride, the others broken pumice stone moistened with conc. sulfuric acid.

The saturators and the halide absorber were in a thermostat mounted on a rocking device which oscillated about 30 times a minute. The U-tubes for absorbing the water were outside the thermostat. To avoid possible condensation of water vapor, the tube connecting the last saturator with the U-tubes was kept at a slightly higher temperature than the thermostat by passing a small electric current through a wire wound around it.

Finally, the air passed through a roughly calibrated gas meter. This served to indicate the approximate rate of flow of the air through the system.

On account of the oxidizing action of air upon hydriodic acid, nitrogen was employed as the inert gas in the experiments upon this halide. An apparatus similar to that described by Hulett[2] was employed to reduce to a negligible amount the small percentage of oxygen which the commercial nitrogen contained. Before starting a run the air was swept out of the preliminary saturating apparatus and the connecting tube by means of hydrogen, and a current of this gas was passed through the saturator while the hydriodic acid was being transferred to it. In spite of these precautions the more concentrated solutions became slightly brown before the run was started. During the run the oxidation did not increase to a noticeable extent. In order to determine the maximum effect of oxidation a modified run on 9.3 molal acid was made. In this run the precautions observed in filling the apparatus were not taken and the small amount of oxygen contained in the nitrogen was not removed. The gases from the saturator were passed over carbon tetrachloride contained in the absorbing device. The iodine taken up by the carbon tetrachloride amounted to less than 2% of the total iodide found in the absorber at the end of a regular experiment in which acid of the same concentration was employed. In the latter run the amount of oxidation, as indicated by the color of the solution in the saturator was very much less, the resulting error was certainly less than 0.5%.

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[1] This Journal, 37, 309 (1915)

[2] *Ibid.*, 27, 1415 (1905)

In each of the determinations from 50 to 200 liters of air or nitrogen was passed through the system at rates of 7 to 10 liters per hour. At the end of a run the water absorbers were immediately removed and weighed. The solution in the absorber for the hydrogen halide was poured into an Erlenmeyer flask, and the absorber rinsed with four 10 cc. portions of distilled water; this was shown by tests to be ample to remove all halides. When more than about 0.001 equivalent of halide was present in the absorber, it was determined by the standard method of Gooch. Smaller amounts were determined by the method of McLean and Van Slyke,[1] modified as follows. The halide was precipitated in the presence of a known amount (about one gram) of free nitric acid with an excess of 0.025 *N* silver nitrate solution. After coagulation of the colloidal precipitate had been accomplished by shaking the mixture for a few seconds with two drops of caprylic alcohol, the silver halide was removed by filtration through a Gooch crucible. The excess silver nitrate contained in the filtrate was titrated with 0.01 *N* potassium iodide which had been standardized against the silver nitrate solution. Just before titration 4 cc. of trisodium citrate solution[2] was added for each gram of free nitric acid present. Under these conditions, using starch as an indicator, 0.05 cc. of 0.01 *N* potassium iodide gave distinct color change in 150 cc. of solution.

The concentrations of the hydrochloric and hydrobromic acid solutions whose vapor pressures were determined were found by titration against sodium carbonate. In the case of the hydriodic acid, the concentrations were determined by diluting a weighed amount of acid and titrating the resulting solution against 0.05 *N* silver nitrate solution, by the method of McLean and Van Slyke. The acid solutions employed were obtained by redistilling Baker's c. p. acids, the first and last portions of the distillates being rejected.

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[1] This Journal, 37, 1128 (1915).

[2] McLean and Van Slyke, *Loc cit.*

4. Preliminary Experiments.

Preliminary experiments were made to determine the effectiveness of the saturator and of the absorber. To test the degree of saturation of the air with the hydrogen halide, three runs were made employing the same solution of hydrochloric acid. In each of these runs about 100 liters of air was passed through the system at rates of 5, 10 and 20 liters per hour, respectively. The vapor pressures thus determined agreed with one another to within 2%. To further test the saturation, the preliminary saturating device was temporarily removed and a run made. The value given by this experiment was within 1% of those previously found. The experiments of Washburn and Heuse[1] show that the method of saturating the air with water vapor is efficient and reliable. They passed air through similar saturators at a much faster rate than that used in this investigation and obtained equilibrium conditions. Thus in one experiment air was passed at a rate of 27 liters per hour. The difference between the vapor pressures of water as given by two such saturators in series was 0.02%.

The efficiency of the absorber was demonstrated by the fact that, when 60 liters of air was passed through the apparatus at a rate twice as great as that used in the final experiments, no determinable amount of chlorine was found in a second absorber. It was further tested by examining the water contained in the water saturator. If the hydrogen halide were not completely removed from the air during its passage through the absorber containing the sodium hydroxide solution, it would be largely taken up by the following part of the system, namely, the water saturator. After 3 runs had been made without renewing the water in the saturator, it was tested and found to yield less than 0.002 milli-equivalent of halide.

In order to make certain that none of the acid solution was being carried from the saturator to the absorber in the form of spray, a run was made in which the saturator contained 4 molal potassium chloride. Although the air was passed through the system at a rate greater than that employed in the final experiments, no trace of halide was found in the absorber at the end of the run.

Differential manometers placed between various parts of the system showed that any pressure differences in the system were less than 0.1 mm. of mercury. In the final experiments the manometers were not used.

[1] This Journal [illegible]

5. Method of Computing the Results.

In computing the results from the experimental data it is assumed that the water vapor and the hydrogen halide gas at the low pressures involved obey the perfect-gas law. The error introduced by these assumptions is less than the errors of the experimental method.

The vapor pressure p_1 of hydrogen halide in its solution, which is equal to the partial pressure of hydrogen halide in the air in equilibrium with it, is given by the familiar expression

$$p_1v_1 = N_1RT. \tag{1}$$

Here N_1 is the number of mols of hydrogen halide contained at the temperature T in the volume of air v_1 which passed through the hydrogen halide saturator. For the water vapor we have the similar expression

$$p_2v_2 = N_2RT. \tag{2}$$

Here v_2 is the volume of the air as it passes through the saturator for water vapor. The volumes v_1 and v_2 differ slightly, for, though the total pressure in the two saturators is substantially the same (as shown by the differential manometers), the partial pressure of the air is $p_a - p_s - p_1$ as it leaves the hydrogen halide saturator, and $p_a - p_2$ as it leaves the water saturator, p_a being the barometric pressure and p_s the vapor pressure of water above the acid solution. Since the quantity of the air is the same in the two cases, its pressure-volume product must be the same, *i. e.*,

$$(p_a - p_s - p_1)v_1 = (p_a - p_2)v_2. \tag{3}$$

By combining Equations 1, 2 and 3, the following expression for p_1 results:

$$p_1 = p_2\frac{N_1}{N_2}\cdot\frac{(p_a - p_s - p_1)}{(p_a - p_2)}$$

For p_2, the vapor pressure of pure water, the values 23.76 mm. and 31.85 mm. were employed at 25° and 30°, respectively. The vapor pressure of water in equilibrium with the acid solution p_s, was in the case of hydrogen chloride, interpolated from the values given by Linhart.[1] For solutions of hydrobromic acid and of hydriodic acid it was assumed, because of lack of the desired data, that the values of p_s are the same as those for hydrochloric acid of the same concentrations. It was determined from the freezing-point curves for solutions of these 3 halides and also from a comparison of the vapor pressure results obtained in this investigation, that the maximum error in the values thus chosen for p_s is 20%. Such an error would cause an error of less than 0.3% in the values calculated for the partial pressures.

6. Experimental Data and Computed Vapor Pressures.

The experimental data and the calculated vapor pressures are given in Table I. In this table M is the concentration of the acid solution

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[1] This Journal, 39, 2607 (1917)

TABLE I.—EXPERIMENTAL DATA ON THE VAPOR PRESSURE OF THE HYDROGEN HALIDES ABOVE THEIR AQUEOUS SOLUTIONS

M.	C	$E \times 10^{3}$	W	$p_{\text{mm.}}$	$D_{\text{mm.}}$	$D\%$
Hydrochloric Acid at 25°						
3 240	3 021	0 0521	2 870	0 00780	0 00002	+0 3
3 952	3 656	0 0982	2 453	0 01724	0 00006	—0 3
5 041	4 570	0 3118	2 416	0 0557	0 0003	+0 5
5 364	4 834	0 3259	1 781	0 0791	0 0027	+3 5
6 018	5 359	0 7085	2 063	0 1487	0 0066	+4 6
6 270	5 559	0 7552	1 895	0 1727	0 0067	—3 7
6 457	5 706	0 983	2 073	0 206	0 007	—3 3
7 148	6 238	1 069	1 206	0 385	0 013	—3 3
8 157	6 980	3 685	1 602	0 999	0 035	+3 6
8 950	7 546	4 920	1 175	1 819	0 031	—1 6
9 960*	8 248	9 643	1 043	4 012	0 071	—1 7
9 071*	8 256	9 116	0 961	4 117	0 007	+0 2
9 990	8 270	19 483	1 985	4 260	0 079	+1 9
			Average percentage deviation =			2 8
Hydrochloric Acid at 30°						
5 569	4 990	0 4137	1 620	0 148		
7 329	6 364	1 095	0 895	0 712		
8 726	7 364	6 768	1 510	2 61		
9 286	7 764	6 789	1 139	3 47		
Hydrobromic Acid at 25°						
5 851	5 076	0 0130	3 695	0 00153	0 00024	+16
6 394	5 482	0 0165	2 250	(0 0032)		(+35)
7 632	6 374	0 0333	2 497	0 0058	0 0006	—10
8 315	6 845	0 0617	2 338	0 0115	0 0003	—3
8 325	6 850	0 0866	2 811	0 0134	0 0016	+12
9 143	7 393	0 118	2 217	0 0232	0 0023	—10
9 655	7 730	0 249	2 337	0 0466	0 0037	+8
10 440	8 221	0 460	2 261	0 0888	0 0009	+1
10 950	8 546	0 705	2 155	0 143	0 001	—1
			Average percentage deviation =			7
Hydriodic Acid at 25°						
5 971		0 0041	3 529	0 00051	0 00008	—16
6 038		0 0033	2 696	0 00053	0 00007	—13
6.171		0 0064	2 974	0 00093	0 00022	+23
7 586		0 0195	2 388	0 00355	0 00025	—7
8 697		0 1187	2 692	0 0192	0 0010	+5
9 251		0 167	2 687	(0 0271)		(—98)
9 332		0 335	2 729	0 0536	0 0046	+8
9 776		0 586	2 728	0 0937	0 0018	—2
			Average percentage deviation =			10

* Solutions saturated with calomel

expressed in mols per 1000 g. of water, C the concentration in mols per liter, E the equivalents of halide found in the absorber, W the weight in g. of water of the hydrogen halide in millimeters of mercury, D_{mm} and D % the deviations, in mm. and in percentages, of the individual values from the smooth curve obtained by plotting the experimentally determined values of log p against those of M.

The irregularities in the above results arise to a large extent from the analytical methods employed. Thus, the percentage error in the determination of the concentration of the acid employed, is increased 6 to 10 fold when expressed as a deviation of the vapor pressure results. At the lower concentrations, particularly in the case of hydrogen bromide and iodide, the minute amounts of halide present in the absorber could be determined with an accuracy of about 10% only.

The vapor pressures for hydrogen chloride at 25° given in Table I are two or three times as great as those interpolated at corresponding concentrations from Gahl's data. It is impossible to point out specific causes of error in Gahl's method because he apparently did not test the efficiency of his saturators and because he gives no data showing the concordance of his results, nor details such as the rate of flow of gases through his apparatus, the volume of gases passed, etc. As already stated, Ellis pointed out that Gahl's results were not consistent with the electromotive force data.

In order to test the accuracy of the values found by Dolezalek, the 4 determinations at 30° were made. The results obtained are more consistent with each other than are Dolezalek's, and on the average differ from the values interpolated from the data of that investigator by about 40%; in fact, at certain concentrations the values given by Dolezalek for 30° are approximately equal to those interpolated for 25°, from the results of this investigation. The above vapor pressures at 30° were compared with those at 25° by the aid of the van't Hoff equation. The average differences between the 4 values obtained at 30° and the corresponding results calculated from the experiments at 25°, is 8%. This is not large considering the character of the data, particularly the uncertainty of the thermochemical values involved.

TABLE II. VAPOR PRESSURES OF THE HYDROGEN HALIDES AT 25° AT ROUND CONCENTRATIONS.

Mols per 1000 g H_2O	Vapor pressure in mm.		
	HCl	HBr	HI
4.0	0.0182		..
5.0	0.0530		..
6.0	0.140	0.00151	0.00057
7.0	0.348	0.00370	0.00182
8.0	0.844	0.0089	0.0065
9.0	1.93	0.0226	0.0295
10.0	4.20	0.059	0.132
11.0	.	0.151	.....

The vapor-pressure data at 25° were interpolated to round concentrations by means of the curves employed for determining the deviations. The interpolated results are given in Table II.

7. Comparison with Electromotive-Force Data.

The vapor-pressure data for hydrogen chloride may be compared with the electromotive-force measurements of hydrochloric[1] acid concentration cells in the following manner. The free-energy decrease attending the transfer of 1 HCl from a solution c molal to a solution 0.1 molal[2] is given by the expression

$$-\Delta F = EF \tag{4}$$

where E is the electromotive force of a cell in which the above change in state takes place and F the value of the faraday. The same free-energy decrease may be expressed also by means of the equation

$$-\Delta F = RT \log_e p/p_{0.1} \tag{5}$$

where p and $p_{0.1}$ are the vapor pressures of hydrogen chloride above its c molal and its 0.1 molal solutions, respectively

From Equations 4 and 5 the relation

$$EF = RT \log_e p/p_{0.1}$$

follows. Hence

$$\log_{10} p = \log_{10} p_{0.1} + \frac{EF}{2.303RT} \tag{6}$$

Therefore the graph obtained by plotting values of $\log_{10}p$ against corresponding values of E should be a straight line having the slope

$$F/2.303\ RT.$$

The desired values of E may be readily calculated from the results of Ellis[3] and of Linhart.[3] Both of these investigators determined the electromotive force at 25° of cells of the type

$$H_2(1\text{ atm.}),\ HCl\ (c\text{ molal}),\ Hg_2Cl_2 + Hg$$

over a considerable concentration range. By subtracting the electromotive force of the cell in which the concentration is c molal, from that of the similar cell in which the concentration is 0.1 molal, the quantity E which is to be substituted in Equation 6 is obtained. These values were calculated and plotted against concentrations expressed as mols per 1000 g. of water. The results of Ellis and of Linhart are in good agreement with each other. From this graph values of E corresponding to the concentrations at which the vapor pressures were experimentally determined were read off and plotted against values of $\log_{10}p$.

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[1] There are no corresponding data for hydrobromic acid or hydriodic acid concentration cells

[2] The results could be referred to a solution of any other concentration within the range of the E. M. F. data, the concentration 0.1 molal offers particular advantages for the free energy calculations which follow.

[3] *Loc. cit.*

At concentrations below about 7.15 molal the agreement is entirely satisfactory, the points lie on a straight line having the slope required by Equation 6. Above this concentration they continue to lie on a smooth curve but not upon the straight line. This deviation can be accounted for only by assuming an error in either the electromotive force or the vapor-pressure data or in both.[1] This portion of the curve is founded upon 2 electromotive-force measurements and 5 vapor-pressure determinations. Of the latter 3 at 10 molal have an average deviation of 1.3%. An error of 10% in the vapor-pressure data, of 3 millivolts in the electromotive-force data or of 1% in the concentration of the acid would explain the discrepancy.

Because of the uncertainty of the data for the solutions more concentrated than 7.15 molal, only the results obtained within the range in which the electromotive force and vapor-pressure data show good agreement were employed to calculate $p_{0.1}$, the vapor pressure of hydrogen chloride above its 0.1 molal solution; this value is employed in the free energy calculations which follow. From the experimental result at each of the 8 concentrations below 7.15 molal, the vapor pressure of 0.1 molal hydrogen chloride calculated by means of Equation 6. The mean of these values is 2.23×10^{-6} mm.; the average deviation from the mean is 3.4%, the probable error 1.2%.

8. The Free Energy of Formation of Hydrogen Chloride and of the Hydrogen Halides in Solution.

The free energy of formation of hydrogen chloride may now be obtained by adding to the free energy of 1 HCl in 0.1 molal solution, which has been computed by Ellis[2] to be —34, 330 calories, the free energy increase which results when the pressure is increased from that which the hydrogen chloride has above its 0.1 molal solution to a pressure of one atmosphere. This free energy increase is found by the equation $\Delta F = RT \log (760/2.23 \times 10^{-6})$ to be 11,630 calories. Hence the free energy of formation at 25° of hydrogen chloride is —22, 700 calories.

The free energies of the hydrogen halides in solutions of various concentrations at 25° are given in Table III. The values for hydrogen chloride up to and including 4 molal[3] were interpolated from the results of Ellis.

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[1] In the electromotive-force determinations the hydrochloric acid solutions which were in contact with the calomel electrodes were saturated with calomel. Experiments showed that the effect of dissolved calomel upon the vapor pressure of 10.0 molal hydrochloric acid was negligible. See Table I.

[2] *Loc. cit.* Table X.

[3] Free energies for solutions more dilute than 0.1 molal may be computed from the electromotive-force measurements of Noyes and Ellis (THIS JOURNAL, 39, 2532 (1917).

TABLE III.—FREE ENERGIES OF HYDROGEN HALIDES IN SOLUTION AT VARIOUS CONCENTRATIONS AT 25°.

Mols per 1000 g H_2O.	Free energy in calories		
	HCl.	HBr.	HI
0.1	—34330	—27550	—15260
0.5	—32500		
1.0	—31590		
2.0	—30510		
3.0	—29690		
4.0	—29100		
5.0	—28365		
6.0	—27790	—20365	—8035
7.0	—27250	—19830	—7360
8.0	—26725	—19300	—6600
9.0	—26235	—18760	—5700
10.0	—25775	—18190	—4815
11.0		—17635	..
Free energy of formation of gaseous halide	—22700	—12592	+310

At the higher concentrations the free energies were computed by adding to the free energy of 1 HCl(*g*), the free energy of expansion from a pressure of one atmosphere to a pressure equal to its partial pressure in the solution in question. The free energies of hydrogen bromide and of hydrogen iodide were calculated in a similar manner; the free energies of formation of 1 HBr(*g*) and of 1 HI(*g*) were taken as —12592 and +310 calories, respectively.[1] The free energy of hydrogen bromide in 0.1 molal solution was computed from the results of Lewis and Storch,[2] that of hydrogen iodide from the free energy of the iodide ion.[3]

9. Summary.

1. Determinations have been made of the vapor pressures of hydrogen chloride, of hydrogen bromide and of hydrogen iodide above their aqueous solutions between the concentrations 3.2 and 10.0 molal, 5.8 and 11.0 molal, and 6.0 and 9.7 molal, respectively, at 25° and of hydrogen chloride between 5.5 and 9.2 molal at 30°.

2. By the method employed partial pressures as small as 0.001 mm. were determined with an accuracy of a few per cent.

3. The vapor-pressure measurements of hydrochloric acid solutions between 3.2 and 7.15 molal are in good agreement with the electromotive-force data for hydrochloric acid concentration cells.

4. The free energy of formation at 25° of hydrogen chloride is —22,700 calories.

5. The free energies at 25° of the halide acids in aqueous solutions of various concentrations are given.

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[1] Lewis and Randall, THIS JOURNAL, 36, 2259 (1914); *Ibid.*, 38, 2348 (1916).

[2] THIS JOURNAL, 39, 2544 (1917).

[3] Lewis and Randall, THIS JOURNAL,

[CONTRIBUTION FROM THE WOLCOTT GIBBS MEMORIAL LABORATORY OF HARVARD UNIVERSITY.]

THE DIELECTRIC CONSTANTS OF TYPICAL ALIPHATIC AND AROMATIC HYDROCARBONS, CYCLOHEXANE, CYCLOHEXANONE, AND CYCLOHEXANOL.

BY T. W. RICHARDS AND J. W. SHIPLEY

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This investigation is part of an extended research which has as its object the study of the properties of a large number of related carbon compounds.

The simplest method for the measurement of dielectric constants depends upon the comparison of the capacities of a given condenser when air, a standard substance, and the substances to be studied are successively placed between the condenser plates. As developed by Nernst[1] and his pupils the essential apparatus consists of a bridge, in which capacities as well as resistances are balanced. Into one arm of the bridge are placed two condensers in parallel, one consisting of two brass plates between which slides a movable glass plate whereby it is possible to vary the capacity of the condenser at will, the other of a vessel containing the liquid to be measured, between two metal plates. Into the other arm of the bridge is placed a balancing condenser. The details of this method have been so frequently described that it is unnecessary to repeat them here.[2]

The principal objection to the method lies in its narrow application, since a sharp minimum on the telephone receiver is not obtainable when a good conductor fills the vessel. The method was nevertheless chosen for the present work, because the major portion of the liquids to be studied were very poor conductors. For such it offered the readiest and most exact method for determining their dielectric constants.

The apparatus used was based upon that described by Nernst, but the arrangement was modified so as to secure greater percentage accuracy. The most important modification consisted in the use of larger and more similar balanced capacities in each arm of the bridge, thus gaining better minima of sound in the telephone, and a larger range of the insulating glass plate of the variable condenser. The larger capacities consisted of very narrow troughs, each possessing two nickel-plated brass plates about 0.6 mm. apart, firmly cemented upon glass plates and held apart as well as retained in position by strips of glass around the edges, the whole presenting a deep, very thin layer of dielectric between the condenser plates, which possessed considerable electrical capacity. The use of similar troughs of this kind on each side of the bridge greatly promoted precision of the end-point. In the first arrangement (troughs E and E′) the glass strips forming the edges of each trough intruded somewhat between the brass plates, but this intrusion was undesirable for several reasons, causing an uncertainty in the capacity, doubt as to the attainment of exactly the same surface on successive fillings, and several minor difficulties. Accordingly, the first troughs thus constituted were soon rejected, and most of the work was done with two pairs of troughs (F and F′, G and G′) in which the opposing surfaces of the metal plates were entirely free from cement. The strips of glass which held the metal plates apart were several millimeters from their edges, and were cemented only to the glass plates. Two sizes were made, the area of the plates in F and F′ being each 7.5 × 4.6 cm., and the area of the plates in the smaller pair of troughs (G and G′) being 7.0 × 4.0 cm. The cement used was a commercial cement made entirely of inorganic materials and intended for cementing glass and porcelain. After having been cemented, the troughs were dried for 10 days at a temperature of about 90°. This cement was perhaps not the best conceivable, but it was entirely insoluble in the liquids employed, and the electrical capacities of the troughs thus made remained essentially the same at the end as it was at the beginning of the work, thus showing that the apparatus had served its purpose satisfactorily.

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[1] Nernst, *Z. physik. Chem.*, **14**, 622 (1894).

[2] B. B. Turner, *Ibid.*, **35**, 385 (1900). More fully in *Dissertation*, Göttingen, 1900; Philip, *Z. physik. Chem.*, **24**, 19 (1897); Bädeker, *Ibid.*, **36**, 305 (1901); Cauwood and W. E. S. Turner, *J. Chem. Soc.*, **107**, 276 (1915), etc.

As is well known, the use of a suitable interrupter and telephone receiver is of great importance in this method. Instead of using the ordinary conductivity-telephone receiver, we tested several commercial telephone receivers intended for long distance wireless telegraphy, and found by experience one which worked admirably in conjunction with our interrupter and gave results of great precision, being sensitive to within 0.1 mm. on the condenser-graduation. The interrupter was of the type used by earlier experimenters—a fine, platinum wire stretched to suitable tension between two vertical posts, the wire being wound in the middle for a few millimeters with fine, iron wire, to be attracted by the solenoid magnet. This was regulated so that the pitch was exceedingly high, almost at the upper limit of audibility.

In each case the two similar troughs, one to contain the substance to be studied, and the other to serve as a balance or "tare-capacity," were placed in a carefully insulated constant temperature air bath, which consisted of a moderately roomy rectangular glass vessel within a second larger glass vessel, also rectangular, supported upon the bottom of the latter by two glass "horses." The space between the two rectangular vessels was usually filled with water, to help in maintaining constant temperature. The condenser-troughs stood vertically edge to edge on the bottom of the air-chamber (the inner rectangular vessel) and during an experiment did not in any respect change their other or to the different parts of the apparatus. In order to eliminate as far as possible the effects of changing humidity upon the troughs, they were surrounded by a dry atmosphere. This was obtained by passing a stream of dry air through a coil of tubing in the bottom of the outer vessel and down inside of the inner one. The air escaped in a series of holes from a horizontal branch lying along the bottom of the air chamber, and by preventing the access of the atmosphere of the laboratory obviated the necessity of an elaborate air-tight covering for the inner box.

In a few cases where the amount of material was very small the old style of trough like that employed by Nernst (designated Z) was employed. Such results are, therefore, no better as regards precision than the work of that investigator, but within their limit of error they are exactly identical with those obtained with the larger capacity, as is shown by the results for cyclohexane. Since the more important reading is that of the variable condenser, the precision of the work is proportional to the range of this instrument, assuming equality of definiteness of sound in the telephone. The range was about 6-fold greater with trough G and 7-fold greater with trough F than in the case of the Nernst form Z.

The thermostats of the heating system of the laboratory kept the room temperature constant to within about 0.5° on each side of the average, 20°. This was quite near enough, since no appreciable change in the capacity of the system was observed by changing the temperature by one degree,[1] except in the case of cyclohexanol, which will receive special discussion in another paper.

The whole apparatus was rested on sheets of ebonite; and the air bath was mounted on two glass rods lying on ebonite, and was arranged symmetrically with regard to the variable condensers. No change whatever was made in the relation of the parts during a determination. The carrier containing the liquid whose dielectric constant was being determined was undisturbed even while being filled; it was charged and emptied by means of a small pipet and dried between trials by a current of dry air. In this way the effect of changing outside capacity was eliminated, for the readings for air, benzene, and liquid whose dielectric constant was unknown were made successively without disturbing any part of the system. It was found that this procedure was absolutely essential in order to obtain consistent results; strict compliance with this precaution is the key to success.

As usual, the relative capacities of the several parts of the system varied slightly day by day, for no obvious reason. The variation was sometimes as much as one mm. on the condenser scale; but very seldom was any important variation observed during the time required for a full determination. If any difference between the initial and final readings for air (always taken both before and after each determination) was observed, the determination was discarded. Probably the variations were due to change in the outside or balancing capacities with change of humidity, or to changing electrical conditions. The dry air of the steam-heated laboratory is especially favorable to work of this kind, and we had less trouble in regard to accidental changes of capacity than usual.

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[1] See also Cauwood and W. E. S. Turner, *J. Chem. Soc.*, 107, 278 (1915).

The water surrounding the air bath was temporarily replaced by oil without causing any change in the capacity of the system. Neither were the slight daily changes in outside capacity thereby eliminated. Owing to greater viscosity, its tendency to cling to glass, and its lower specific heat, oil was less convenient than water.

Usually only the left variable condenser of the Nernst apparatus was varied, in order to restrict as much as possible any change in the relative positions of the parts of the apparatus.

The connections, which were arranged as symmetrically as possible, keeping the wires insulated and far apart, are indicated by the accompanying diagram. Here A is the interrupter; B and B′, the two large resistances composed of a solution of boric acid and mannite; C and C′, two other similar resistances forming the other arms of the bridge; D and D′, variable condensers; E and E′, two narrow troughs serving, one as container for the liquid to be studied, and the other as balancing capacity (which were in the constant air chamber); and T, the telephone receiver.

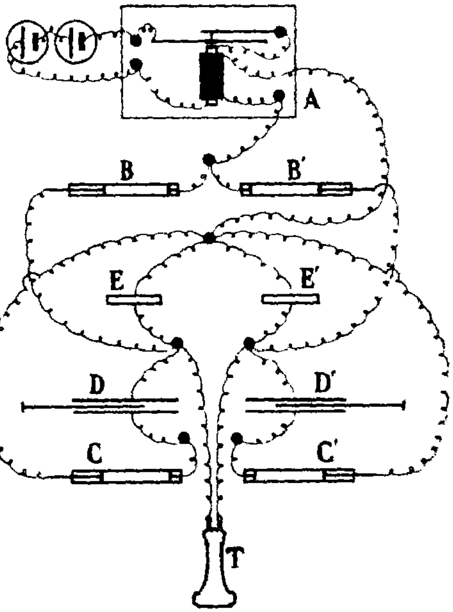

Fig. 1.

The variable condenser scale D was calibrated in the following manner: A strip of glass (a microscope mounting slide) large enough when introduced between the plates of the condenser to cause a change in capacity equal to about one cm. on the variable condenser scale was alternately slipped in and out of the trough E, each time in precisely the same position. By moving the right hand variable condenser, this constant capacity could be measured on any part of the left whose scale was thus calibrated along its entire length. A curve, plotted with corrections as ordinates and the scale readings as abscissas, yielded the corrections applied to the results.

The gravest source of error in using the apparatus was found to result from altering the relative positions of the electrodes in the liquid resistances of the Wheatstone bridge when a substance possessing considerable conductivity was introduced into the containing trough. The capacity of these liquid resistances between the electrodes changed considerably when the electrodes approached each other very closely, and also when the conductivity of the liquids in these tubes was increased. The latter fact was determined by adding sodium chloride to the boric acid-mannite solution and reading the change in capacity on the variable condenser scale as the relative position of the electrodes in the liquid resistance was altered.[1] The phenomena were studied quantitatively, and the exact range over which the resistances could be varied without appreciably changing the capacity was noted. The details need not be discussed here; it is enough to say that no determinations involving conditions beyond the permissible range were accepted as valid.

Each of the resistances C and C′ (in the diagram) possesses two tubes, a wide one for coarse adjustment, and a capillary one containing only a fine wire for adjustment, or for very great resistances. In the cases of most of the substances studied the fine wire electrode alone was used, and so low was the conductivity that a change of only a few millimeters was needed to balance the conductivity of the liquid in the trough. This produced only a very small change in the capacity.

The standard substances used for comparison in this research were benzene and ether. Toluene also served as a standard of reference, since its dielectric constant is accurately known. It was especially used in testing the efficiency of the troughs, being convenient on account of its lesser volatility. The results were calculated by means of the following equation:[2]

$$D_s = (D_{\text{benzene}} - 1)\frac{S_1 - S}{S_2 - S} + 1$$

where D_s is dielectric constant of the substance; S_1, the corrected reading on condenser for substance in trough; S the corrected reading for air in trough; and S_2 the corrected reading for benzene in trough. The dielectric constant of benzene at 20° was taken as 2.286, according to B. B. Turner's careful investigation already quoted.[3] When ether was used as a standard, instead of $D_{\text{benzene}} = 2.286$ must be substituted $D_{\text{ether}} = 4.355$, and S_2 becomes the reading for ether.

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[1] For another form of liquid resistance, which to some extent obviates this difficulty, see Nernst, *Wied. Ann.*, **66**, 611 (1897)

[2] Nernst, *Z. physik. Chem.*, **14**, 622 (1894).

[3] B. B. Turner, *Loc. cit.* His determination was at 18°; to this was applied a correction of —0.0007 per degree. See Ratz, *Z. physik. Chem.*, **19**, 104 (1896); also Cauwood and Turner, *Loc. cit.* Nernst found a lower value, 2.255 at 17°, but Turner's results are more recent and appear to be more accurate.

Source and Preparation of Materials.

Benzene.—The best commercial C. P. benzene was further purified by shaking with 4 portions of conc. sulfuric acid, washing several times with water, shaking with mercury, washing yet again, and distilling. After two crystallizations the product was dried over sodium. Thorough drying is essential. No change in the dielectric constant was observed throughout the course of the research and the value for this sample was the same as that given by two more carefully purified products prepared for another purpose.[1]

Ether of good quality was washed several times with water, shaken with mercury until the surface of the mercury was no longer blackened, and again washed. After drying over sodium it was distilled and kept tightly stoppered, over sodium in the dark. At the end of the research a portion of this sample was redistilled and its dielectric constant determined. No change from that of the original sample could be observed.

Toluene (the purest obtainable commercial material) was shaken with sulfuric acid, washed, shaken with conc. sodium hydroxide solution, again washed, and then shaken with mercury. After filtering, the toluene was dried over sodium and distilled. The product all came over between 110.1–110.6° (786 mm. pressure) and no difference in the dielectric constant of the different fractions could be detected. That fraction distilling between 110.4–110.5° was used for the various determinations of toluene.

Hexane.—Normal hexane (synthesized in this laboratory) dried over sodium, was distilled at a temperature of 69.2° (758 mm. pressure) the entire product distilling within 0.3°. The dielectric constant was determined before and after the last distillation.

Heptane.—A quantity of "heptane" of questionable purity, prepared by a well known German firm from petroleum, was dried over sodium and fractionated. The dielectric constants of the several fractions were determined in succession, as will be seen, all the fractions gave essentially the same value. The average boiling points of the samples I, II, III and IV were, respectively, 100°, 98°, 97.6° and 96.5°. Probably the result represents an average value for several heptanes.

Octane.—A quantity of 2,2,3-trimethyl pentane prepared by Dr. Latham Clarke was redistilled from sodium. The fraction 110.8–111.4° (765 mm. pressure) was used.

Decane.—Commercial diisoamyl was dried over sodium and fractionated. Two fractions, boiling, respectively, between 159.5–159.7° and 160.1–160.3° (761 mm. pressure) were studied.

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[1] Richards and Shipley, This Journal, 36, 1826 (1914).

Xylene.—A sample of German "xylol" probably a mixture of *o*-, *m*- and *p*-xylene, dried over sodium, was fractionated, and the several fractions were determined. These fractions boiled over the following ranges: Xylene I, 137–137.7°; Xylene II, 137.7–138.8°; Xylene III, 138.8–139.6°. No differences in their dielectric constants were found. In addition to this unsatisfactory material a sample of the best obtainable *m*-xylene was dried over anhydrous copper sulfate and distilled, collecting the fraction between 138.8–139.2° (741 mm. pressure). As will be seen, it gave essentially the same result.

Besides toluene and the *m*-xylene already mentioned, 5 other aromatic hydrocarbons with saturated side-chains were obtained in a high state of purity. These had been prepared synthetically at Harvard for the express purpose of determining their physical constants and were the same samples as were used in the work on compressibility[1] and heat of combustion.[2] They were as follows: *Ethyl benzene* I (Fittig method), b. p. 136.3–136.4°, d_4^{20} 0.8678; *Ethyl benzene* II (Friedel-Crafts method), b. p. 136.4–136.5° (767 mm.), d_4^{20} 0.8697; *Normal propyl benzene*, b. p. 157.9–158.2° (765 mm.), d_4^{20} 0.8617; *Isopropyl benzene* (*cumene*), b. p. 152.6–152.8° (759 mm.), d_4^{20} 0.8620; *Mesitylene*, b. p. 164.8–164.9° (760 mm.), d_4^{20} 0.8634; *Tertiary butyl benzene*, b. p. 168.6–168.7° (759 mm.) d_4^{20} 0.8671.

Cyclohexane.—Very pure cyclohexane was prepared for this research, made from benzene by the Sabatier-Sanderens reduction, and afterwards purified by often repeated recrystallization: (b. p. 81.3–81.5°, f. p. 6.4°, d_4^{20} 0.7791).

Cyclohexanone.—A quantity of this ketone had been prepared for the work on compressibility.[3] (B. p. 155.6–155.7°, 768 mm., d_4^{20} 0.9466.) Ketones are better conductors than the hydrocarbons and their dielectric constants are higher. Few ketones could be determined with our apparatus and of alcohols none but those of large molecular weight had conductivity low enough.

Cyclohexanol, prepared at the same time as the cyclohexanone, was purified by fractionally crystallizing it in the absence of moist air. The freezing point of the best sample was 23.9°. Several samples were used, two of which had freezing points above 20°. Hence the temperature chosen for measurement was 25° in this case. The heat of fusion of cyclohexanol is so low that the presence of a very little water makes a marked depression in the freezing point; exposing to the air for a few minutes lowers its freezing point several tenths of a degree. Probably moisture from the air was not absolutely excluded, so that the results for this substance cannot be considered corresponding exactly to a perfectly water-free sample. Fortunately the presence of a little water in this case ap-

[1] Richards and Shipley, THIS JOURNAL, 38, 989 (1916).

[2] Richards and Barry, *Ibid.*, 37, 997 (1915).

[3] Richards and Shipley, *Loc. cit.*

peared not to affect appreciably the value of the dielectric constant, provided that the measurement was taken several degrees above the freezing point of cyclohexanol.

The Constancy of the Apparatus.

From time to time during the research, determinations of the dielectric constant of ethyl ether and of toluene were made as a check on the constancy of the apparatus. The data below give the results of these determinations, using benzene (2.286) as the standard of reference. Each of the numbers given in the following tables represents a separate filling and adjustment of the apparatus and each is an average of a number of measurements, repeated until the last figure was reasonably certain.[1]

TABLE I.—DIELECTRIC CONSTANTS OF ETHER AND TOLUENE AT 20 0°

Readings (Corrected).

Substance	Trough	Air (S)	Ether (S)	Benzene (S_2)	Dielectric constant
Ether	E	0 92	6 94	3 22	4 366
	E (cover)	1.40	7 39	3 70	4 349
	F	2 78	10 22	5 64	4 345
	G	2 22	7.55	4 26	4 360
	F	2 78	10 21	5 63	4.353
				Ether Average,	4 355
		Air	Toluene	Benzene	
Toluene	E (cover)	1 10	3 72	3 60	2 348
	E	0 33	3 10	3 01	2 329
	F	2 30	5 28	5 17	2.336
	F	2 30	5 28	5 18	2.330
	F	2 30	5 28	5.18	2.330
				Toluene Average,	2 335

Evidently the results are as nearly constant as could be expected. They show that the apparatus is consistent and to be depended upon. Below are given the results for other substances, all referred to the dielectric constant of dry air = 1.000.

TABLE II.—DATA AND RESULTS.

(All at 20° except Cyclohexanol)

Substance	Trough	Corrected reading			Dielectric constant.
		S.	S_1	S_2	
Hexane	F	2 78	4.76	5.68	1.878
	F	2.78	4.76	5.70	1.872
	F	2.78	4 76	5.68	1.878
					Average, 1.876
Heptane I	F	2.70	4.87	5.57	1 972
Heptane II	F	2.70	4.87	5.57	1.972
Heptane III	F	2.70	4.87	5.37	1.972
Heptane IV	F	2.70	4.88	5 57	1.977
					Average, 1.973

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[1] As an example, at random, the following readings were taken in the case of the second experiment with ether: With air, 1.39, 1.40, 1.40, 1.40; with ether, 7.38, 7.39, 7.40, 7.39; with benzene, 3.70, 3.69, 3.70. The averages to the nearest figure in the

TABLE II (*continued*).

Substance	Trough	Corrected reading.			Dielectric constant.
		S	S_1	S_2	
Octane	F	2.80	4.97	5.70	1.962
N-Nonane	F	2.74	4.92	5.64	1.967
4-Methyl octane	F	2.80	4.98	5.70	1.967
4-Methyl octane	F	2.74	4.92	5.64	1.967
2-Methyl octane	F	2.74	4.92	5.64	1.967
2,6-Dimethyl heptane	F	2.70	4.37	4.87	1.989
2,6-Dimethyl heptane	F	2.70	4.38	4.87	1.995
2,6-Dimethyl heptane	F	2.70	4.35	4.87	1.978
2,4-Dimethyl heptane	Z	2.40	2.69	2.82	1.89
2,4-Dimethyl heptane	Z	2.40	2.69	2.82	1.89
2,5-Dimethyl heptane	Z	2.40	2.69	2.82	1.89
Decane I	F	2.30	4.44	5.18	1.955
Decane II	F	2.30	4.44	5.18	1.955
Decane II	F	2.30	4.44	5.18	1.955
Decane II	F	2.30	4.45	5.18	1.960
					Average, 1.956
Xylene I	F	2.70	5.77	5.57	2.375
Xylene II	F	2.70	5.77	5.57	2.375
Xylene III	F	2.70	5.77	5.57	2.375
					Average, 2.375
Xylene	F	2.30	5.40	5.17	2.389
	F	2.30	5.38	5.18	2.375
	F	2.30	5.38	5.18	2.375
	F	2.30	5.37	5.18	2.371
					Average, 2.378
Ethyl benzene I	G	2.62	5.18	4.84	2.482
Ethyl benzene II	G	2.62	5.19	4.85	2.482
Ethyl benzene III	G	2.62	5.18	4.84	2.482
					Average, 2.482
N-Propyl benzene	G	2.53	4.88	4.74	2.367
	G	2.53	4.89	4.76	2.361
					Average, 2.364
Cumene	G	2.21	4.43	4.26	2.393
(isopropyl benzene)	G	2.52	4.95	4.74	2.408
					Average, 2.400
Mesitylene	G	2.53	4.86	4.74	2.356
Tert butyl benzene	G	2.30	5.40	5.18	2.384
	G	2.30	5.39	5.18	2.380
	G	2.30	5.41	5.18	2.388
					Average, 2.384
Cyclohexane	E	0.95	2.90	3.32	2.058
	E	0.95	2.89	3.32	2.053
	Z	2.40	2.75	2.82	[2.07]

TABLE II (*continued*).

Substance.	Trough	Corrected reading S	S_1		S_s	Dielectric constant
Cyclohexanone	Z	3.26	9.21	Ether	4.42	18.2
	Z	3.28	9.85		4.57	18.1
	Z	3.24	7.82		4.13	18.3
	Z	3.24	7.81		4.13	18.2
					Average,	18.2
Cyclohexanol at 25°	Z	2.70	6.99	Benzene	3.09	15.2
	Z	2.70	7.00		3.10	14.8
	Z	2.70	7.00		3.09	15.2
	Z	2.70	7.00		3.10	14.8
					Average,	15.0

TABLE III.—COMPARISON OF RESULTS WITH THOSE OF FORMER EXPERIMENTS.

Substance	Earlier results at various temperatures: Temp. Degrees	Observer	Dielectric constant	Present results at 20°. Dielectric constant
Benzene	20.0	B. B. Turner[b]	2.286	Standard[a]
Ether	18.0	B. B. Turner[b]	4.368	4.355
N-Hexane	17.0	Nernst[c]	1.88	1.876
N-Hexane	12.4	Landolt & Jahn[d]	1.86	1.876
Heptane (average)			.	1.973
N-Octane	17.0	Nernst[c]	1.95	1.962
2,2,3-Trimethyl pentane				1.962
N-Nonane				1.967
4-Methyl octane				1.967
2-Methyl octane				1.967
2,6-Dimethyl heptane				1.987
2,4-Dimethyl heptane				1.89
2,5-Dimethyl heptane				1.89
Decane	13.8	Landolt & Jahn[d]	1.966	1.956
Toluene	19.0	Drude[e]	2.31	2.335
Toluene	14.4	L. & J.[d]	2.375	. .
M-Xylene	18.0	B. B. Turner[b]	2.376	2.377
Xylene (mixture of isomers)				2.375
Ethyl benzene	17.0	Nernst[c]	2.42	2.482
Ethyl benzene	14.6	L. & J.[d]	2.42	. .
Propyl benzene	13.8	L. & J.[d]	2.35	2.364
Cumene (isopropyl benzene)	17.0	Nernst	2.37	2.400
	18.0	Drude[e]	2.42	. .
Mesitylene	14.2	L. & J.[d]	2.30	2.356
Tertiary butyl benzene			.	2.384
Cyclohexane	25.0	Cauwood and W. S. E. Turner[f]	2.07	2.055
Cyclohexanone			.	18.2
Cyclohexanol				15.0 (25°)

[a] In each case the last figure is more or less uncertain—often not over one unit.

[b] B. B. Turner, *Z. physik. Chem.*, **35**, 385 (1900).

[c] Nernst, *Ibid.*, **14**, 622 (1894); *Wied. Ann.*, **60**, 600 (1897).

[d] Landolt & Jahn, *Z. physik. Chem.*, **10**, 289 (1892).

[e] Drude, *Ibid.*, **23**, 267 (1897). *Ann. d. Phys.*, [4] **8**, 336 (1902) (improvement of method).

[f]

Evidently our results for substances already investigated by others agree essentially in most cases with the earlier results, especially with those of B. B. Turner, whose investigation was a model of care and accuracy. This leads us to hope that the other determinations, which give for the first time the dielectric constants of a number of typical carbon compounds, are also trustworthy.

The data are not plentiful enough to form the basis of far-reaching conclusions concerning the effect of structure on dielectric constant, but nevertheless at least one outcome is unmistakable, namely, the fact that both in the aliphatic and the aromatic series the substitution of the methyl group for hydrogen has usually but slight tendency to change the dielectric constant. With the higher members, this effect is less than that which is produced by variation in structure. Thus the values for hexane, heptane, octane, the average of the nonanes, and decane are, respectively, 1.88, 1.97, 1.96, 1 94, 1.96, whereas the range among the nonanes alone is from 1.89 to 1.99 Some of the nonanes with side-chains have a higher, some a lower, dielectric constant than normal nonane. The aromatic hydrocarbons, as is well known, all possess higher dielectric constants than the aliphatic hydrocarbons. Benzene, toluene, *meta*-xylene, and mesitylene give, respectively, 2 29, 2 33, 2 38, 2 36. Aromatic hydrocarbons with more complicated side-chains (*n*-propyl-, isopropyl-, and tertiary-butyl benzene) give about the same values (respectively, 2.36, 2.40 and 2.38) with the incomprehensible exception of ethyl benzene, which gives the highest of all those studied (2.48). The effect of the benzene ring is evidently to increase the dielectric constant by about 0.4, or 20% of its value for the paraffins.

We are indebted to the Carnegie Institution of Washington for financial assistance in the prosecution of this work.

Summary.

1. A modified form of the Nernst apparatus is described. Percentage error was much decreased by the use of larger, suitably balanced condenser-troughs.

2. The dielectric constants of 21 organic liquids have been determined, some of them for the first time. The values for aromatic hydrocarbons average about 20% higher than for aliphatic hydrocarbons.

CAMBRIDGE, MASS

[Contribution from the Research Laboratory of Physical Chemistry, Massachusetts Institute of Technology, No 116.]

HYDROGEN OVERVOLTAGE. II. APPLICATIONS OF ITS VARIATION WITH PRESSURE TO REDUCTION, METAL SOLUTION AND DEPOSITION.

By D A MacInnes and A. W. Contieri

Received October 7, 1919.

1. The Variation of Hydrogen Overvoltage with Pressure.

In a previous article[1] it was shown that, for low current densities, hydrogen overvoltage, E, is related to the radius r, of the bubbles formed on an electrode, the pressure p, and the surface tension γ, by the expression

$$2FE = \frac{3RT}{pr}\gamma. \tag{1}$$

For platinized platinum electrodes, at one atm. pressure, the agreement of observed overvoltages, and those calculated from determinations of r, was found to be quantitative. Also, it will be recalled, the variation of the overvoltage with pressure, for mercury, lead and nickel electrodes, was shown to be in the direction predicted by Equation 1. The nearly quantitative nature of this agreement was, however, not pointed out. If Equation 1 is valid, a plot of the variation of the overvoltage with the pressure should be a hyperbola, provided that the bubble radius r is a constant. In Fig. 1, where overvoltages are plotted as ordinates and pressures as abcissas, the continuous line represents the measurements of Goodwin and Wilson on a nickel electrode, and the dotted line shows the calculated values, the overvoltage at one atm. having been used in obtaining the values at the lower pressures. Although these curves have nearly the same form, the overvoltage changes with pressure somewhat more slowly than is predicted by the theory. This small difference may be due to a slight increase in the size of the bubbles as the pressure decreases or, more probably, to an increased stirring effect, due to the larger number of bubbles formed at the lower pressures from a given weight of gas. It is interesting to observe that this theory of overvoltage, which was based mainly on observations, at atmospheric pressure, on platinized platinum electrodes, can be used to explain phenomena obtained with electrodes having much higher overvoltages, and at widely varying pressures.

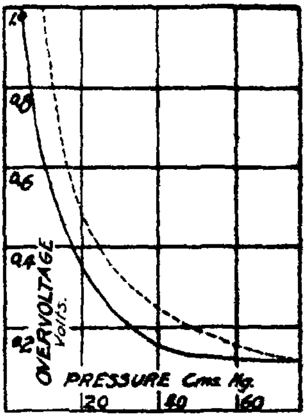

Fig 1.

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[1] This Journal, 41, 194 (1919).

2. Applications of the Variation of Hydrogen Overvoltage with Pressure.

The variation of overvoltage with pressure being established, theoretically and experimentally, it becomes important to study the effect of pressure on chemical processes involving the evolution of hydrogen in order to observe whether, in each case, changes in these processes can be predicted from the variation of the overvoltage. Three such chemical processes are: (*a*) the solution of metals in electrolytes, (*b*) reduction, in acid solutions, by metals, and (*c*) the electro-deposition of metals.

(*a*) The Role of Hydrogen Overvoltage in the Solution of Metals. The Variation of the Rate of Solution with Pressure.—When a piece of a metal is placed in a solution of an electrolyte there is a tendency for the metal to form ions, *i. e.*, to split into ions and electrons. With metallic iron, for instance, the following reaction tends to take place:

$$Fe = Fe^{++} + 2\epsilon \qquad (2)$$

However, no chemical action will follow unless another reaction, involving the absorption of the electrons, can also occur. In the absence of oxidizing agents the only possible reaction is

$$2H^{+} + 2\epsilon = H_2 \qquad (3)$$

and this will take place only when the potential between the metal and the electrolyte is greater than the lowest potential at which Reaction 3 can proceed in the system. Any factor which tends to decrease the velocity of Reaction 3, *i. e.*, which increases the overvoltage, will, of course, decrease the rate of solution of the metal

Watts and Whipple[1] have found that, contrary to statements in the chemical literature, a decrease of the gaseous pressure will produce a reduction of the rate of solution of metals in acids. These workers, however, attribute the decreased corrosion in the acid solutions which were under reduced pressure, to the absence of oxygen. As it seemed probable to us that this effect is, largely at least, due to an increase of the overvoltage with decreased pressure, we repeated the experiments on zinc, cadmium and iron, taking care to exclude oxygen from all the solutions. In these experiments two test pieces of each metal were cut so as to expose very nearly the same area, and weighed. The pieces were then placed in separate test-tubes containing the same volume of acid from which the air had been removed by boiling under reduced pressure. One of these tubes was then connected to a vacuum pump, and a stream of hydrogen at atmospheric pressure was passed through the other tube. After the reaction had proceeded for some hours the test pieces were removed, dried, and again weighed. A few typical results of such experiments are given in Table I.

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[1] *Trans. Am. Electrochem. Soc.*, 32, 257 (1917)

TABLE I.

The Solution of Metals in Normal Sulfuric Acid.

Metal.	Time Hours.	Loss in wt. per sq cm. area Mg.	
		At. atm. pressure.	At 8 cms. Hg
Zn…	6	15.4	9.90
Fe…	4	11 01	6 52
Cd…	7	0 42	0.42

Since, at the lower pressures, a given mass of gas occupies a larger volume than at atmospheric pressure, the agitation of the solutions was greater when under partial vacuum, but, at least in the cases of zinc and iron, the rate of solution was much decreased. Cadmium was, however, but slowly acted upon by the acid and no bubbles were observed to leave its surface, the liberated hydrogen evidently dissolving and diffusing away. Under these conditions no change of the overvoltage with pressure is to be expected, as no (liquid-gas) surface energy is involved. On comparing our results with those of Watts and Whipple it seems probable that, although the effect described is responsible for the greater portion of the change of the rate of solution with pressure, oxygen also aided in the solution of the metals in the experiments they carried out at atmospheric pressure.

If a piece of platinum is attached to a sample of cadmium the latter will enter solution rapidly enough to cause an evolution of gaseous hydrogen. In this case we found that the rate of solution of the metal was decreased from 4 mg. to 1.4 mg. per sq. cm. in 23 hours by decreasing the pressure from atmospheric to 11 cm. Hg. The test pieces were prepared by soldering a given length of platinum wire to each sample of cadmium. The soldered joint was covered with paraffin while in the acid.

Copper, although normally below hydrogen in the electromotive series, will dissolve with an evolution of hydrogen when placed in a strong potassium cyanide solution. As is well known, this is due to a very low copper ion concentration in the solution, caused by the formation of complex ions. In this case also the rate of solution was greatly decreased by lowering the pressure. At atmospheric pressure 1.7 mg. per sq. cm. dissolved in 5 hours. This was decreased to 1.0 mg. per sq. cm. in the same time by reducing the pressure to 11 cm. of Hg.

It also follows from the theory that an increase of pressure above that of the atmosphere will result in a decrease in overvoltage. The rate of solution of a metal, when the reaction is accompanied by a liberation of hydrogen, should thus be increased by an increase of pressure. To test this point two nearly identical samples of sheet iron were placed into tubes, A and B, containing the same volume of 0.5 N hydrochloric acid. The air was pumped out of Tube A and the reaction was allowed to proceed at ordinary placed a simple pressure indicator consisting of a capillary tube closed at one end and with a drop of mercury initially near the other end. After replacing the air in Tube B with hydrogen it was sealed up, and the gas generated by the progress of the reaction caused a rise of pressure to nearly 10 atmospheres. After 16 hours, the losses in weight of the pieces of iron in Tubes A and B, were respectively, 18.1 and 34.2 mg. per sq. cm., the latter figure being, of course, the result of pressures varying from 1 to 10 atm. It was interesting to note that, throughout the experiment, there was no apparent change in the rate of the reaction as judged by the rate of evolution of hydrogen bubbles, although when the pressure in the Tube B reached its maximum, a bubble of a given size in the latter Tube represented 10 times the mass of hydrogen that it did in the Tube A. As nearly as could be estimated, the bubbles were of the same size in both tubes.

(*b*) **The Variation, with the Pressure, of the Efficiency of Reductions by Metals.**—When the reduction of a compound is carried out in aqueous solution with the aid of a metal above hydrogen in the electromotive series, the efficiency of the reduction is usually decreased because of the evolution of hydrogen. For example, when a piece of iron is placed into a slightly acidified solution of ferric chloride the metal dissolves according to the reaction

$$Fe = Fe^{++} + 2\epsilon. \tag{2}$$

The two reactions that compete for the liberated electrons are

$$Fe^{+++} + \epsilon = Fe^{++} \tag{3}$$

and

$$2H^{+} + 2\epsilon = H_2. \tag{1}$$

Here we can predict that a decrease of pressure will, by increasing the overvoltage, reduce the velocity of Reaction 1, with the result that the efficiency of the reduction represented by Reaction 3 will be increased. Several series of experiments were carried out in which pieces of iron, of constant area, were placed in contact with acidified ferric chloride solutions at a series of pressures. The results of one series are given in Table II.

TABLE II

Pressure (Cm Hg)	Equivalents of $FeCl_3$ reduced in 90 minutes.
8 0	0 415
8.5	0.400
17.0	0.363
20.2	0.259
22.0	0.280
25.6	0.240
32.0	0.220
36.8	0.095
76.0	0.078

The solution contained 0.625 mole per liter of ferric chloride and 0.17 mole per liter of hydrogen chloride, 20 cc. being used in each experiment. The pieces of iron exposed 3.08 sq. cm. area to the solution. The amount of ferric iron remaining after each reduction was determined with the help of a colorimeter. The figures on Table II are also plotted in Fig. 2 in which ordinates represent ferric iron reduced and abscissas pressures in cms. Hg. Although the points are scattered the drift is clearly very similar to that of the overvoltage-pressure curve given in Section 1 The continuous line in the figure is a hyperbola. A number of attempts were made to secure data that would yield smoother curves, but without success, the difficulty being, in all probability, the variability of the surface of the iron. As suggested, the rapidity and efficiency of the reduction appears to be closely related to the overvoltage of the iron. Very similar results to the above were obtained with zinc as the reducing metal.

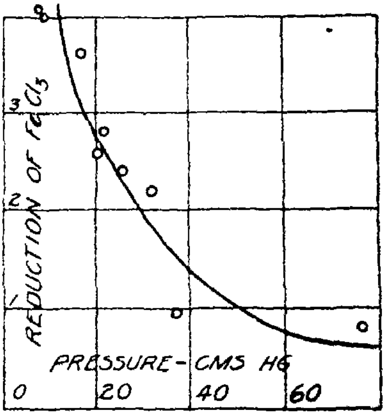

Fig 2

It appears probable that the speed and efficiency of a large class of reductions can be increased by carrying out the reactions under diminished pressure. Further work on this subject will be carried out in this laboratory.

(*c*) **The Effect of Variation of Hydrogen Overvoltage on the Efficiency of the Electrolytic Deposition of Metals.**—If hydrogen were evolved at a cathode at its reversible potential, under all conditions, no metal higher than hydrogen in the electromotive series could be deposited electrolytically from aqueous solutions. The fact that metals as high in the series as zinc can be obtained in this way is due, of course, to the fact that the overvoltages of the metals are of the same order of magnitude as the potentials between the metals and the electrolytes from which they are deposited. In all such depositions, however, the current efficiencies are decreased because of the evolution of hydrogen. It is to be expected, therefore, that any factor which tends to increase hydrogen overvoltage will increase the efficiency of the deposition of a metal above hydrogen in the electromotive series.

To determine whether the effect of reduction of pressure is in the direction predicted, a study was made of the deposition of zinc from ($^1/_2$ molar) zinc sulfate solution. Two cells, each containing an anode and cathode of zinc, were placed in series in a circuit containing a copper coulometer.

One of the cells was arranged so that the electrolysis could be carried out under reduced pressure. The two cathodes, which were made as nearly alike as possible, were weighed before and after each electrolysis. The current density was kept at 3 milliamperes per sq. cm. Table III gives the efficiencies at a series of pressures.

TABLE III.

The Effect of Pressure on the Efficiency of the Deposition of Zinc.

Pressure, cm. Hg	76	13	11	7	6
Efficiency, % . . .	75	81.0	92.4	94.5	97.5

The efficiency at atmospheric pressure is the mean of 4 values differing by several per cent. As in the case of reductions at the surfaces of metals, it is difficult to obtain reproducible results. The increase of efficiency with a decrease of pressure is, however, unmistakable. A similar, although smaller, effect with decrease of pressure, was found in the deposition of iron.

It should be emphasized here that the effects described in this paper are obtainable only for comparatively slow reactions and for low current densities. A violent evolution of hydrogen gas apparently breaks down the layer of supersaturated hydrogen solution which is responsible for the overvoltage.

3. Further Discussion of Overvoltage Fluctuations.

A topic that deserves more consideration than was accorded it in the previous communication is the somewhat puzzling observation that the formation of a single minute bubble can determine the potential at an electrode with an area several thousand times the surface covered by the bubble, as was the case in the experiments described. Fig. 3 represents a typical fluctuation of the overvoltage with time. As explained in the former article, at point *b* a bubble has separated, leaving a nucleus attached to the electrode, which is surrounded by a solution of hydrogen in equilibrium with bubbles the size of the one which has just separated. At *a'*, however, a concentration is reached at which the nucleus can grow, after which a very rapid drop in the potential is observed. This drop is due, in all probability, to an ionization of a portion of the dissolved hydrogen (according to the reaction $H_2 = 2H + 2\epsilon$) and the reappearance of an equivalent amount of hydrogen in the bubble. It will be recalled that as the bubble grows the equilibrium concentration of dissolved hy-

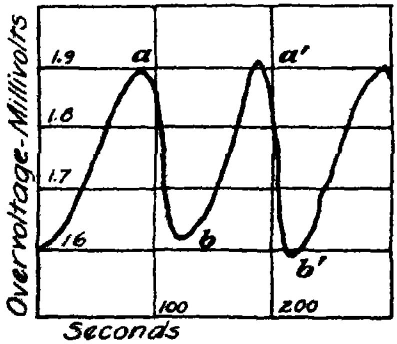

Fig. 3.

drogen decreases, since the "solubility" of small bubbles is greater than that of larger ones. The electrolyte immediately surrounding the growing bubble is, therefore, less concentrated than at points on the surface of the electrode removed from the bubble. These differences of concentration produce short-circuited concentration cells, the operation of which results in the formation of hydrogen ion from dissolved molecular hydrogen at points where the latter is more concentrated, and the reverse reaction at the bubble or in the adjacent electrolyte.

4. Summary.

The increase of hydrogen overvoltage with diminished pressure is shown to follow, in a nearly quantitative manner, from the theory advanced by MacInnes and Adler.

A study has been made of the effect of change of gaseous pressure on several chemical processes involving the evolution of hydrogen. The changes in rates of reaction and in reaction efficiencies were found in each case to be in the directions which follow from the change of hydrogen overvoltage with pressure, *i. e.*, a decrease of gaseous pressure produces (*a*) a decrease of the rate of solution of metals in electrolytes, (*b*) an increase in the efficiency of reductions by metals, and (*c*) an increased efficiency of metal deposition.

The theory explaining the fluctuation of overvoltage accompanying the evolution of a single bubble from a platinum electrode is more fully discussed.

CAMBRIDGE, MASS

[CONTRIBUTION FROM THE WOLCOTT GIBBS MEMORIAL LABORATORY OF HARVARD UNIVERSITY.]

THE EFFECT OF PRESSURE, AND OF DISSOLVED AIR AND WATER ON THE MELTING POINT OF BENZENE.

BY THEODORE W. RICHARDS, EMMETT K. CARVER AND WALTER C. SCHUMB.

Received October 16, 1919

The need of a large number of accurately determined fixed points for standardizing thermometers is too well understood to need comment. The transition temperatures of the hydrated salts seem to be the points best suited for this purpose, although the freezing points of pure liquids are also convenient. To give a useful fixed point the liquid adopted must not only be one that may be easily and surely purified, but it must also have a high latent heat of fusion. This last is important for two reasons: because such a substance sooner compensates for loss of heat through the walls of the container or gain from stirring, and because the effect of impurities on the freezing point is inversely proportional to the latent heat of fusion.

Although benzene is less satisfactory in these respects than water, nevertheless it is by no means to be rejected as a means of fixing a thermometric point.

With this in mind, one of us, with the assistance of J. W. Shipley,[1] recently determined with care the freezing points of two carefully prepared samples of pure benzene (from coal tar and from benzoic acid) and found the same very constant point for each, namely, 5 483° ± 0.002°. The measurements were made in the Beckmann apparatus with carefully calibrated thermometers.

The point thus determined is evidently of sufficient constancy to serve the purpose in mind; nevertheless it is not, of course, the true triple point of benzene. The determination was made under atmospheric pressure; moreover, as J. Meyer[2] has rightly pointed out, the liquid contained dissolved air. For the object sought, these circumstances make no difference, if only the pressure and saturation of dissolved air are constant. The essential feature is convenient and exact reproducibility of the point. Meyer's objection that the concentration of the dissolved air varies is (as will be shown) not well taken, since during the production of the amount of solid required for a satisfactory observation, enough air is displaced from the crystals to saturate fully the remaining liquid. Hydrogen from the decomposition of water by the sodium used in drying could not have been present, since it must have escaped during the distillation.

In order to place the matter in a more satisfactory situation, the effect of the dissolved air has been studied, as herewith detailed. The procedure adopted was first to determine the freezing point of benzene under its own vapor pressure, and then, to admit dry air at atmospheric pressure and take the temperature when the benzene became saturated.

To protect the thermometer from the change in pressure when air was admitted, it was immersed in mercury in the inner open tube of a double-walled test-tube, whereas the benzene was placed in the outer compartment, between the walls. Just above the mercury in the inner tube was a layer of carbon tetrachloride which served to protect the mercury from loss of heat, and the whole apparatus was protected from too rapid heat-exchange by means of an air jacket. An iron stirrer plated with silver, in the benzene, was lifted and dropped by means of an electromagnet operated by a metronome and relay. The whole was placed in a thermostat at about 5.3° to 5.6°.

The apparatus was filled through a ground joint, which was then closed and sealed with mercury. A trap caught any benzene which had distilled into contact with the stopcock leading to the pump. At first a

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[1] T. W. Richards and J W. Shipley, This Journal, 36, 1825 (1914).

[2] J. Meyer, *Z. physik. Chem.*, 90, 721 (1915). See also Garelli and Falcioli, *Atti accad. Lincei*, [1] 13, 110 (1904); also Prytz and Holst, *Wied. Ann.*, 54, 130 (1895).

Beckmann thermometer was used, but was found unsatisfactory owing to the uncertainty of the stem correction. In later determinations an old, very accurate and sensitive Baudin thermometer with a large bulb was used. Finally the point on the international scale was determined by standard Baudin thermometers Nos. 15200 and 15276.

Determinations were made as follows: The apparatus was filled about half full of benzene, which was frozen solid The disengaged air was pumped off (the evacuation being continued to minimum pressure), and the benzene was melted and frozen again. After a second evacuation very little, if any, air remained. Finely divided crystals, highly satisfactory for the purpose, were produced by supercooling the liquid benzene several degrees and stirring. The automatic stirring was continued, and the solid phase augmented; but until there was so much solid benzene that the motion of the stirrer was prevented, the temperature remained unchanged. This proved that no air remained, since otherwise the temperature would have fallen slowly as the liquid diminished. By varying the rate of stirring over a wide range it was shown that the heat of stirring had no appreciable effect on the apparent melting point.

When the triple point had thus been fixed, and the quantity of crystals best suited to give a constant point had developed, air dried over sulfuric acid was admitted The freezing point immediately rose about 0.028°, since benzene freezes at a higher temperature under high pressure than under low pressure. As the stirring continued, the temperature fell because of the air dissolved, at first rapidly, and then more slowly, in a well-defined curve, of which a typical graph follows.

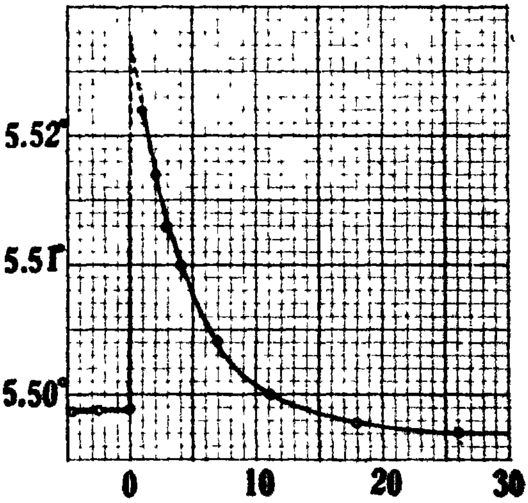

Fig 1.—Typical diagram showing fall of temperature caused by solution of air in pure benzene.

Ordinates represent temperatures, abscissas represent time in minutes. The initial maximum temperature is attained only with complete absence of stirring, and then only for a brief time. During the trial indicated the stirring was continuous and equable.

In this manner, after a few preliminary trials, the following 5 successive determinations were made. The 3 samples of benzene referred to in the table were prepared as follows: For

Expts. 1 and 2 the benzene was shaken with 5 successive portions of conc. sulfuric acid. Then followed several washings with a solution of sodium hydroxide and several successive portions of water. It was subsequently dried over calcium chloride and sodium, distilled, recrystallized 5 times, and kept over sodium. Successive portions of this metal were needed to eliminate all the water. The material used for Expts. 3 and 4 was identical with Shipley's Sample C, and that used in the fifth determination was identical with Shipley's Sample B. The former had been crystallized 4 times and the latter 6.[1] Both had been kept 3 years over sodium, and all were distilled directly into the freezing-point apparatus. Below are recorded the results, corrected to the hydrogen standard of temperature as given by the mean of the readings of thermometers Baudin 15200 and 15276, making due correction for the effect of changing atmospheric pressure on the thermometer bulb and all other known causes of error.

TABLE I.—DIFFERENCE BETWEEN FREEZING POINT IN VACUUM AND IN AIR

	Degrees centigrade		Difference
	In vacuum	In air	Vac. Air
(1) Benzene as described above	5.504	5.502	0.002
(2) Benzene as described above	5.502	5.498	0.004
(3) Shipley's synthetic benzene (4th)	5.498	5.496	0.002
(4) Shipley's synthetic benzene (4th)	5.500	5.496	0.004
(5) Shipley's coal-tar benzene (6th)	5.499	5.497	0.002
Average	5.5006	5.4974	0.003

The absolute value will be considered in detail later. The important outcome of figures given in the table is the fairly consistent evidence that the melting point of benzene saturated with air under atmospheric pressure is 0.003° lower than the true triple point of pure benzene, and that the difference is reasonably constant, and trustworthy.

This small correction (0.003°) is made up of two almost equal opposing large corrections. The presence of dissolved air lowers the freezing point, but the pressure of the atmosphere increases it. The latter of these two effects may be computed from the well known equation of Clapeyron: $dT/dP = T\Delta v/L$. According to the carefully executed determinations of J. Meyer, one g. of benzene on melting takes in 30.48 average calories, and increases its volume by 0.1333 cm.[2] This gives $dT/dp = 0.0295$ degree per atmosphere. Tammann's direct measurement[3] between 0 and 500 atmospheres gives $dT/dp = 0.028$ degree per atmosphere, but on making due allowance for curvature of the line depicting the change with pressure, it would appear that his result at atmospheric pressures must almost exactly agree with that computed above. The average change of pressure in the 5 experiments was from 35.4 mm. (the pressure of benzene vapor at its triple point) to 762.4 mm (the average barometer) or 727 mm. This change should then alter the freezing point by (727/760)0.0295° = 0.0282°.

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[1] THIS JOURNAL, 36, 1830 (1914).

[2] J. Meyer, *Z. physik. Chem.*, 72, 246 (1910).

[3] Tammann, *Krystallisieren und Schmelzen*, Leipzig, 1903, p. 197; see also *Wied. Ann.*, 66, 486 (1898).

Taking 0.028° as the pressure effect, 0.031° is computed (by the addition of 0.003°) as the depression of the freezing point due to air dissolved in benzene under atmospheric pressure. The weight of air dissolved in the benzene may be estimated from this result by the familiar equation, $w = MW\Delta t/k$, which gives 0.017 g. or 13 cc. of air dissolved in 100 cc. of benzene. It was found by Just[1] that 11 cc. of nitrogen at 760 mm. pressure dissolved in 100 cc. of benzene at 20°, but he made no trial with oxygen. Probably oxygen is somewhat more soluble than nitrogen, hence Just's result is of the same order as ours. The estimate of 63.5 cc. of air per 100 g. of benzene (corresponding to a depression of 0.14° in the freezing point) made by Meyer,[2] is evidently excessive. Meyer's conclusion rested on only a single experiment, made as a side issue in a research having another object, and no evidence is afforded that water was excluded from the benzene in this experiment, an especially insidious source of error in cases like this, as will be shown.

Evidently the melting point of benzene saturated with dry air, under atmospheric pressure, should be an unusually constant point, being much less affected than most freezing points through change of pressure. A rise in the barometer, for example, produces a rise in freezing point through increase of pressure but is accompanied by a proportional increase of dissolved air; each of the opposing almost equal corrections is augmented to almost the same extent. A change of $^1/_4$ of an atmosphere would be needed to change the freezing point of the air-saturated liquid by as much as 0.001°.

As already stated, the graph above indicates that saturation with air is attained rather quickly by freezing benzene agitated by a splashing stirrer. But, on the other hand, is there danger of supersaturation? Liquids are well known to become easily supersaturated with gases, and it is not impossible that benzene saturated with air might become supersaturated as it becomes partly solidified. The ultimate constancy of the freezing point of benzene saturated with air as found both in the earlier research and in the present one shows, however, that the supersaturation is adequately relieved by suitable stirring.

As already stated, another possible source of error or uncertainty in the freezing point of benzene is the presence of water. This is a danger to be especially feared in taking the freezing point of any non-aqueous liquid below the dew point of the air of the laboratory, since water then readily condenses and dissolves in the other liquid. Hence, experiments were instituted in order to determine the effect on the freezing point of benzene of saturation with water, as well as to estimate cryometrically the extent of its maximum solubility at the freezing point.

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[1] Just, *Z. physik. Chem.*, 37, 361 (1901).

[2] J. Meyer, *Ibid.*, 72, 238 (1910).

The literature on the subject is widely divergent in its verdict. One of the early papers, by Herz,[1] states that 0.211 volume of water are taken up at 22° per 100 volumes of benzene (about 87.6 g.). This would correspond to a depression of nearly 0.7° in the freezing point. From our own results, as will be seen, it must be clear that this result is far too large. One cannot help thinking that according to his method of experimentation (which consisted in dropping water into benzene until an excess appeared) an unnoticed film of water must have clung to the glass of the vessel containing the benzene Considerably better, but still possibly somewhat subject to the same cause of error, were the results of Groschuff.[2] He found that 100 g. of benzene dissolves 0.03 g. of water at 3°, and 0.061 g. at 23°, from which we may conclude that at 5.5° about 0.04 g. of water is taken up, corresponding to a depression of about 0.13°.

A safer method seems to be the determination of the effect of water in excess on the freezing point of benzene. According to a recent statement by Wm. J. Jones,[3] Dr. N. V. Sidgwick states that the freezing point of water-saturated benzene is about 0.1° below that of pure benzene. Our own experiments verify this statement, as is seen by the following figures for two separate trials.

	Arbitrary Beckmann	Standard Baudin No 13,276
Temperature of freezing before addition of water, degrees	4.403	5.485 (cor'd)
Temperature of freezing when saturated with water, degrees	4.310	5.389
Difference, degrees	0.093	0.096
		Mean 0.095

If the cryoscopic constant for benzene is taken as 5000, this would correspond to a solubility of 0.034 g. of water per 100 g. of benzene at 5.5°, not far from Groschuff's value.

Evidently an amount of water corresponding to only 1% of the amount in the saturated solution is enough to produce an effect on the freezing point of 0.001°, therefore, great care must be taken to exclude water. Sodium added to benzene containing a trace of water of course evolves hydrogen, and soon becomes coated with sodium hydroxide, when it is less efficient. Accordingly, freshly prepared sodium must be added in successive portions in order to obtain complete dryness in any reasonable time. We found that if perhaps 2 g. of sodium wire is added to 50 cc. of benzene on each of 2 successive days, the liquid is sufficiently dry so that a third portion of added sodium allowed to stand for 2 days more, produces no observable effect upon the freezing point. The fear that sodium thus added in the presence of traces of water might produce a trace of a hydrobenzol does not seem to be substantiated by our experience.

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[1] Herz, *Ber*, 31, 2669 (1898).

[2] Groschuff, *Z. Elektrochem.*, 17, 348 (1911).

[3] W. J. Jones, *J. Soc. Dyers and Colourists*, 35, 46 (1919).

Benzene thus dried must be scrupulously protected from contact with moist air, and all the apparatus which it touches must have been previously heated in a current of dry air in order to exclude traces of water. All these precautions were observed in the work upon the exact freezing point of benzene which follows. No correction was made for the possible solution of carbon dioxide in benzene. The solubility of this gas in the liquid under atmospheric pressure is hardly great enough to make the amount dissolved under its usual partial pressure of 0.0003 atm. appreciable.[1]

The freezing point of benzene as newly found is distinctly higher than those observed by one of us in collaboration with Barry, Davis, and Shipley. Although the object of the present experiments had not at first been to determine the precise value, but only the effect of air, nevertheless the difference obviously suggested further research. Accordingly very careful new absolute determinations of the freezing point of benzene were made, taking account of all the precautions suggested in the foregoing pages.

In repeating the work on the true freezing point of dry benzene saturated with air, a Beckmann freezing-point apparatus was used. The standard Baudin thermometers dipped directly into the mixture of solid and liquid benzene, which was stirred by hand with a platinum-glass stirrer. Air (thoroughly dried by conc. sulfuric acid) was passed continuously through the upper part of the test-tube. The outer bath was kept between 5.0° and 5.5°, approaching the latter point in the final determinations. The distillation of the purified benzene was carried out by electric heating in a glass-stoppered double-necked distilling flask[2] and the distillate could be collected in either one of two receiving test-tubes, at the end of a Y-branched condenser tube, by the expedient of tilting the flask from side to side The test-tube containing the second fraction of the distillate, of which the freezing point was to be determined, was supplied with a cork stopper fitted with the stirrer and standard thermometer all in place, and could be detached from the condenser tube at a ground joint, immediately afterwards being connected to a supply of dry air.

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[1] It was found by Just that benzene dissolves about 2.5 times its volume of carbon dioxide (a result which some results of ours seem to show to be excessive) but even if the gas is as soluble as this, the liquid should take out of ordinary air only about a millionth part of its weight of gas.

[2] T. W. Richards and F. Barry, THIS JOURNAL, 26, 1787 (1910)

Pure coal-tar benzene had been prepared as usual and was further recrystallized 3 times and dried over successive portions of sodium for 2 days at a time. Synthetic benzene had been prepared from benzoate[1] and had been further purified by Dr. Shipley; it was yet further recrystallized 3 times and dried over sodium as in the case of the coal-tar product. For the determination of the ice-point, natural fresh-water ice of good quality was chopped into small lumps, allowed to stand in a beaker until a part of it had melted, then drained and the interstices filled with pure, chilled water before the final reading.

After the purified benzene had stood, as described, over sodium in the distilling flask for several days, it was carefully distilled directly into the test-tube, the first third being collected separately. The benzene all distilled within 0.05°. The test-tube having been disconnected from the condenser at the ground joint and connected to the dry air current, the tube was allowed to cool in an ice bath. By sufficiently supercooling (to about +1°) about a third of the liquid could be instantly frozen in the form of small, flaky crystals; and by further alternately cooling and briefly warming the tube, the quantity of solid could be increased until the whole tube was filled with a thin paste of crystals. The intermittent warming was necessary to cause the solid cakes on the walls of the tube to become disengaged and permit movement of the stirrer. When a paste of the desired consistency had been obtained, the outside of the test-tube was wiped dry and the latter placed in the air-jacket, which was suspended in the cooling bath. Pieces of absorbent cotton were placed about the neck of the test-tube to keep it in place and prevent air currents within the air-jacket. The bottom of the test-tube rested likewise on a pad of cotton. The mixture of solid and liquid benzene was frequently stirred, and the temperature of the thermometer read by means of a cathetometer, which was carefully adjusted. The thermometer was always maintained in a vertical position as tested by a plumb-line, and at a definite distance from the cathetometer objective. In some experiments with Baudin No. 15276 the top of the mercury thread was allowed to just emerge above the top of the cork stopper in the mouth of the test-tube; in one trial (No. 15200 being used) the meniscus was read through the glass of the test-tube, just below the bottom of the stopper; in this case the stem correction was wholly negligible. In all cases the proper stem corrections were calculated, knowing the length and mean temperature of the several portions of projecting thread, both within and above the cork stopper.

[1] Under the kindly undertaken direction of Professor E. P. Kohler.

The freezing point was constant over at least an hour's time in each case, and did not alter appreciably from the initial readings: since the amount of solid had increased in every case by about 25–30%, this constancy is indicative of the purity of the substance.

After a determination had been completed, the benzene was allowed to melt in a current of dry air, and replaced in a bottle over sodium.

The two standard Baudin thermometers used in making the final measurements differed somewhat in their readings when all appropriate corrections had been applied. When a graph of the calibration corrections was made for each thermometer, it was found that unfortunately, from the nature of the curves, just at 5.5° the uncertainty of each was greatest, and in either or both a possible error of 0.003° or more might exist. Therefore the two thermometers were carefully compared with one another, by simultaneously immersing them in a mixture of solid and liquid benzene, and subsequently in a bath of cracked ice and pure water. In this way it was found that No 15200 reads 0.014° higher than No 15276 at 5.5°. The mean value was taken as the best available. This mean is obviously subject to an uncertainty of at least ±0.007 due to the calibration of the thermometers alone, apart from any further uncertainty due to the quality of the benzene

FREEZING POINT OF DRY BENZENE (SATURATED WITH AIR)

Degrees Centigrade

Number of thermometer	No 15 276	No 15,200
(1) Coal tar benzene (Carver's)	5.487	
(2) Coal-tar benzene dried 2 days longer	5.487	
(3) Same as (2)	5.488	5.499
(4)		
(5) Coal tar benzene	5.487	5.501
(6)		
(7) Same as preceding	5.488	5.501
(8)		
(9) Same, one thermometer only used		5.499
(10) Same, one thermometer only used	5.485	
Averages	5.487	5.500

Total average of both thermometers 5.493

The outcome shows that the most probable freezing point of benzene saturated with air is 5.493°, therefore, the true triple point is 5.496°. We are inclined to think that these values (about 0.01° higher than those based on the earlier determination) are the more accurate, since they represent the averages of the readings on two standard thermometers (instead of only one), and since most of the probable errors tend to lower rather than to raise the melting point. Nevertheless as already stated neither of the new values can be considered as certain within a much narrower limit than 0.01°, because of the unfortunate irregularity of the two standard thermometers in this neighborhood. Moreover in spite of the use of many different specimens of benzene, the doubt must always remain as to whether the samples employed were perfectly pure. That our material was purer than the specimen employed by J. Meyer is shown by the fact that our melting point is over 0.05° higher than his (5.44°). The preparation of any organic substance in a state of great purity is difficult, although benzene is more promising in this respect than the great majority, because of its convenient crystallization, its easy preparation, and its considerable stability. For a closer evaluation of the melting point of benzene, a prolonged and laborious investigation would be needful, for which we have not time at present. In the meantime it is safe to say that either the triple point, or the freezing point when saturated with air, is easily attained and very constant.

We are glad to express our obligation to the Carnegie Institution of Washington for pecuniary support in this research.

Summary.

1. Benzene saturated with air under atmospheric pressure melts 0.003° below the true triple point.

2. Benzene thus saturated has its freezing point but little altered by change of pressure.

3. Evidence of an important degree of supersaturation does not appear.

4. The effect of pressure in the absence of dissolved air is shown to alter the freezing point 0.029° per atmosphere.

5. Saturation with water lowers the freezing point of benzene 0.095°.

6. The true freezing point of benzene saturated with air is probably not far from 5.493°, and the true triple point not far from 5.496°.

CAMBRIDGE, MASS.

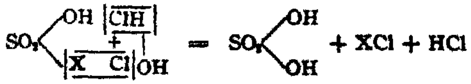
[CONTRIBUTION FROM THE UNIVERSITY COLLEGE OF SCIENCE OF CALCUTTA.]

HALOGENATION. XIX. THE REPLACEMENT OF SULFONIC GROUPS BY CHLORINE AND THE PREPARATION OF ORGANIC CHLORO-DERIVATIVES.

BY RASIK LAL DATTA AND HARAPARBUTTY KUMAR MITTER.

Received April 14, 1919.

It has been found that when a current of chlorine gas is introduced into an aqueous solution of sulfonic acid, the sulfonic group is detached with the simultaneous production of the corresponding chloro-derivative. The reaction that takes place may be represented as follows:



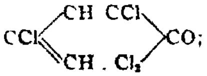
$$\mathrm{SO_2}\left\langle\begin{matrix}\mathrm{OH}\ \boxed{\mathrm{ClH}}\\ +\\ \boxed{\mathrm{X\ \ Cl}}\ \mathrm{OH}\end{matrix}\right. = \mathrm{SO_2}\left\langle\begin{matrix}\mathrm{OH}\\ \mathrm{OH}\end{matrix}\right. + \mathrm{XCl} + \mathrm{HCl}$$

where X represents the organic radical to which the sulfonic group is attached

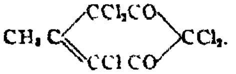
Besides throwing light on a fundamental and general reaction, this method has great practical value. The direct chlorination, in aqueous or glacial acetic acid solution by means of chlorine is generally unsatisfactory as a good deal of substance chars and oxidizes with a considerable diminution in the yield. But with the above reaction there is scarcely any secondary action, and no charring of the sulfonic acid takes place, the chloroderivatives being almost invariably produced in high yield.

It has been found that aromatic bodies which already contain an hydroxy group, as in the case of phenols and oxyacids, exhibit a special facility in the displacement of the sulfonic group by chlorine. The same facility of replacement has also been found in the case of substances which already contain an amido group, as in the case of nitranilines.

The results that have been obtained are interesting. Anisol and phenetol sulfonic acids have given tetrachloro-ketodihydrobenzene,



phenol sulfonic acids yield 2,4,6-trichlorophenol; *o*-cresolo-5-sulfonic acid gives 5-chloro-*o*-cresol, *m*-cresol-6-sulfonic acid and *m*-cresol-2,6-disulfonic acid yield 2,6-dichloro-*m*-cresol; *p*-cresol-3-sulfonic acid gives a trichloro-*p*-cresol, whereas *p*-cresol-3,5-disulfonic acid yields 3,5-dichloro-*p*-cresol. From thymol mono- and di-sulfonic acids, 2,5,6-trichloro-thymol can be obtained, whereas carvacrol-5-sulfonic acid yields trichloro-carvacrol. Orcinol disulfonic acid yields 3,5-diketo-methyl-pentachloro-R-hexane,



From *o*-nitrophenol and *p*-nitrophenol sulfonic acids, 4,6-dichloro-*o*-nitrophenol and 2,6-dichloro-*p*-nitrophenol have been obtained, respectively. *o*-Nitroaniline sulfonic acid and *p*-nitroaniline sulfonic acid yield 4,6-dichloro-*o*-nitroaniline and 2,6-dichloro-*p*-nitroaniline, respectively, whereas *m*-nitroaniline does not give any definite product. *o*-Hydroxybenzoic acid on sulfonation and consequent treatment with chlorine gives 3,5-dichloro-*o*-hydroxybenzoic acid. 2,4,6-Trisulfonic acid obtained from *m*-oxybenzoic acid gives 2,4,6-trichloro-*m*-oxybenzoic acid, and 3-sulfonic-*p*-oxybenzoic acid yields on treatment with chlorine 3,5-dichloro-*p*-oxybenzoic acid.

The phenomena of the replacement of the sulfonic group by chlorine have not been systematically studied, although occasional instances can be found in literature. Kelbe[1] has shown that cymol sulfonic acid yields tetrachlorocymol by the action of chlorine. Meyer[2] has found that *p*-

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[1] *Ber.*, 16, 617 (1883).

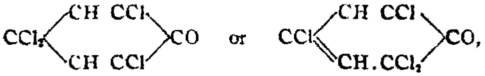
[2] *Monatsh.*, 36, 719 (1915).

dichlorobenzene is formed from *p*-chloro-benzosulfonic acid; and he also obtained α- and β-chloroanthraquinones from the corresponding α- and β-sulfonic acids when acted upon by chlorine. Chlorine replaces the sulfonic group of alizarin-β-sulfonic acid[1] to form chloroalizarin. Farbenfabriken vorm F. Baeyer & Co.[2] and Schillong[3] prepared chloro- and bromoanthraquinones from the corresponding sulfonic derivatives. Haller[4] studied the reaction in oxyanthraquinone. Sudborough and Lakhumalini[5] have studied it in amidobenzene-sulfonic acids.

Experimental.

Anisol.

By the action of chlorine upon an aqueous solution of anisol sulfonic acid, the sulfonic radical is detached with the formation of tetrachloro-keto-dihydrobenzene,



and tetrachloroquinone as a secondary product. The ketochloride together with tetrachloroquinone has been previously prepared by the action of chlorine upon trichlorophenol.[6]

The sulfonic acid is prepared by heating anisol with conc. sulfuric acid on the water bath for about 3 hours when both the *para*- and *ortho*-compounds are formed at the same time.[7] Chlorine was passed through the diluted aqueous solution and after nearly an hour an oil collected. The current of the gas was continued until no more oil was formed. The oil was collected, washed and a part was treated with glacial acetic acid from which it was found to crystallize in colored prismatic needles melting at 122°. This has been identified to be tetrachloro-keto-dihydrobenzene. The glacial acetic acid solution of the substance acts upon the skin.

In order to study the mode of the reaction the experiment was repeated and the solution exhaustively treated with chlorine whereupon the oil formed as before, gradually solidified, and copious flakes of yellow shining crystals appeared in the aqueous solution. The floating crystals were collected separately, dried and recrystallized from glacial acetic acid. The crystals do not melt but sublime at high temperature and were identified as tetrachloroquinone. The semi-solid mass was found to crystallize well from a mixture of ether and ligroin and was then fractionally crystallized from glacial acetic acid, yielding tetrachloroquinone and a solid melting at 122° which was identified as tetrachloro-keto-dihydrobenzene.

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[1] *D. R. P.* 77179, 78642.

[2] *Brit. pat.* 1822 (1908).

[3] *Ber.*, 46, 1066 (1913).

[4] *Ibid.*, 46, 2703 (1913).

[5] *J. Chem. Soc*, 111, 41 (1917)

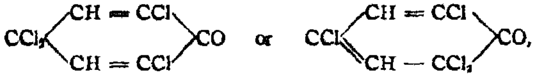
[6] Benedikt, *Monatsh.*, 4, 233 (1883)

[7] Kekulé, *Z. Chem.*, 1867, p. 201; Cahours, *Ann.*, 52, 33 (1844).

The simultaneous formation of the above two substances may be explained by the assumption that anisol sulfonic acid is hydrolyzed to phenol which yields trichlorophenol, and the latter is further chlorinated to tetrachloroquinone and tetrachloro-keto-dihydrobenzene.

Phenetol.

By the action of chlorine upon an aqueous solution of phenetol sulfonic acid, the sulfonic group is detached with the formation of tetrachloroquinone, and tetrachloro-keto-dihydrobenzene,



as a secondary product. The keto-chloride and the tetrachloroquinone were previously prepared by the action of chlorine upon trichlorophenol.[1]

The sulfonic acid is prepared by the action of conc. sulfuric acid upon anisol and then heating on a water bath when both the *para-* and *ortho-*compounds are simultaneously formed.[2] Chlorine was passed through the warm dilute aqueous solution of the sulfonic acid when after nearly an hour an oil was found to collect. The passage of the gas was continued until no further increase in the volume of the oil occurred. The oil was collected, washed and treated with a mixture of ether and ligroin from which it crystallizes as a yellow solid, melting at 115–20°. On treatment with glacial acetic acid it yielded a small amount of white crystals melting at 122°. The substance has been identified as tetrachloro-keto-dihydrobenzene. The glacial acetic acid solution of the substance acts upon the skin.

In order to study the mode of reaction, the previous experiment was repeated and the solution treated exhaustively with chlorine as in the case of anisol, whereupon the oil as before gradually solidified and copious flakes of yellow shining crystals appeared in the aqueous solution. The floating crystals were collected separately, dried and crystallized from glacial acetic acid; they do not melt but sublime at high temperature. These crystals are very characteristic and have been identified as tetrachloroquinone. The semi-solid mass was found to crystallize from a mixture of ether and ligroin, and the resulting crystals were then fractionally crystallized from glacial acetic acid, yielding tetrachloroquinone and a solid melting at 122°, which was identified as tetrachloro-keto-dihydrobenzene.

The simultaneous formation of the above two substances can be explained by the assumption that phenetol sulfonic acid is hydrolyzed to phenol which yields trichlorophenol, and that this is further chlorinated to tetrachloroquinone, and tetrachloro-keto-dihydrobenzene. In the present case tetrachloroquinone forms the main product.

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[1] Benedikt, *Monatsh.*, 4, 233 (1883).

[2] Opl, Lippmann, *Z. Chem.*, 1869, p. 470.

Phenol.

Phenol sulfonic acid on treatment with chlorine forms 2,4,6-trichlorophenol, the sulfonic groups being detached. This 2,4,6-trichlorophenol is also formed by passing chlorine into phenol.[1] It is prepared by the treatment of dil. phenol solution with sodium hypochlorite.[2] Vogel[3] has shown that it is formed by passing chlorine into an aqueous solution of potassium phenol sulfonate.

Into an aqueous solution of phenol monosulfonic acid, preferably freed from any unchanged phenol, chlorine was passed to saturation. The precipitate formed was collected and crystallized from glacial acetic acid, and white needle-shaped crystals obtained, melting at 67-8°, identified as 2,4,6-trichlorophenol. The yield is quantitative.

Into an aqueous solution of phenol disulfonic acid, prepared by sulfonating phenol with 4 parts of fuming sulfuric acid, chlorine was passed. The precipitate formed was separated by suction and crystallized from glacial acetic acid giving white, needle-shaped crystals of 2,4,6-trichlorophenol. The yield is nearly quantitative.

The crude trisulfonic acid obtained by sulfonating phenol with fuming sulfuric acid and phosphorus pentoxide was diluted with water and partially decolorized with animal charcoal. Into this solution, chlorine was passed for a comparatively long time, longer than in the case with phenol mono- and disulfonic acids. The precipitate was collected and crystallized from glacial acetic acid, forming white, needle-shaped crystals of trichlorophenol in small yield.

The yield is quantitative in the case of the monosulfonic acid but in the case of the disulfonic acid it is slightly less, while it is still less in the case of trisulfonic acid, this fact agreeing with the general experience that the greater the number of sulfonic groups to be replaced by chlorine, the greater the difficulty and the smaller the yield.

o-Cresol.

By the action of chlorine upon an aqueous solution of *o*-cresol-5-sulfonic acid, the sulfonic acid radical is detached with the formation of 5-chloro-*o*-cresol. It has previously been prepared by the action of chlorine upon an acetic acid solution of *o*-cresol in presence of iron.[4] It has also been prepared by the action of sulfuryl chloride on *o*-cresol.[5]

The sulfonic acid is prepared by the action of cold conc. sulfuric acid upon *o*-cresol. The 3-sulfonic acid is also produced at the same time, and being much less soluble in water, can thus be separated from the 5-sulfonic acid.[1] Four cc. of *o*-cresol was taken and 4 cc. of cold conc. sulfuric acid was gradually added to it, care being taken to keep it cold. The mixture was shaken from time to time and allowed to stand for some time. The whole of the syrupy liquid was then poured into water and the soluble portion was separated from the insoluble oily portion by means of a separating funnel. The soluble portion containing the 5-sulfonic acid was diluted with water and a current of chlorine was allowed to pass through it until the heavy oil which settles out is no longer formed. The whole was warmed on the water bath and the oil separated by means of a separating funnel, washed with water and dissolved in glacial acetic acid. On cooling and stirring it yielded 1.7 g. of white crystals melting at 47°, which were identified as 5-chloro-*o*-cresol.

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[1] Laurent, *Ann.*, **43**, 209 (1842).

[2] Chandelon, *Bull. soc. chem*, **38**, 123 (1882).

[3] *Z. Chem.*, **1865**, p. 529.

[4] Claus, Jackson, *J. prakt. Chem.*, [2] **38**, 328 (1888).

[5] Penatoner, Condorelli, *Gazz. chim. ital.*, **28**, I, 211 (1898).

m-Cresol.

By the action of chlorine upon an aqueous solution of *m*-cresol sulfonic acids, the sulfonic radicals are detached with the formation of 2,6-dichloro-*m*-cresol. This substance has been previously prepared by passing chlorine into boiling *m*-cresol.[2]

m-Cresol-6-sulfonic acid was obtained by warming *m*-cresol with an equivalent volume of conc. sulfuric acid.[3] A current of chlorine was passed through its aqueous solution for some time when a brown semi-solid mass was precipitated. The solid was collected, washed and crystallized from glacial acetic acid yielding white crystals melting at 45°. The yield from 5 cc. of *m*-cresol was 6.3 g. The substance was identified as the dichloro-*m*-cresol of Claus,[4] melting at 45°. As the substance was found to be identical with that obtained from *m*-cresol-2,6-disulfonic acid by the replacement of sulfonic groups by chlorine as noted below it is evidently 2,6-dichloro-*m*-cresol.

Into an aqueous solution of *m*-cresol-2,6-disulfonic acid prepared by heating one part of *m*-cresol with 6 parts of conc. sulfuric acid to 120–40°,[5] a current of chlorine was passed to saturation. The solid thus formed was collected, washed and crystallized from glacial acetic acid giving white crystals, melting at 45°. The substance was identified as the dichloro-*m*-cresol[6] of Claus; and as the chlorine atoms have replaced both the sulfonic groups in positions 2 and 6, the chloro derivative must be 2,6-dichloro-*m*-cresol. The yield obtained from 5 cc. of *m*-cresol was 8 g.

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[1] Claus, Jackson, *J. prakt. Chem.*, [2] **38**, 333 (1888).

[2] Claus, Schweitzer, *Ber.*, **19**, 930 (1886).

[3] Engelhardt, Latschinow, *Z. Chem.*, **1869**, 622; Claus, Krauss, *Ber.*, **20**, 3089 (1887).

[4] *Ibid.*, **19**, 930 (1886).

[5] Clauss and Krauss, *Ber.*, **20**, 3089 (1887).

[6] *Ibid.*, **19**, 930 (1886).

p-Cresol.

By the action of chlorine upon an aqueous solution of *p*-cresol-3-sulfonic acid, the sulfonic group is detached with the formation of a 2,3,6- or 3,5,6-trichloro-*p*-cresol, whereas 3,5-disulfonic acid yields 3,5-dichloro-*p*-cresol when similarly treated.

p-Cresol-3-sulfonic acid was prepared by the action of fuming sulfuric acid upon *p*-cresol[1] in requisite proportions in the cold. A current of chlorine was passed through the diluted solution for a long time when it yielded a small amount of a product which on recrystallization from glacial acetic acid was found to melt at 85–6°. This has been proved to be trichloro-*p*-cresol by an analysis for chlorine:

Subs., 0.0574 AgCl, 0.1274

Calc for $C_6H(CH_3)(OH)Cl_3$. Cl, 50.35 Found 50.78

The only trichloro-*p*-cresol known is 2,3,5-trichloro-*p*-cresol which melts at 66–7°, which cannot be identified with the substance obtained above. Hence this substance may be either 2,3,6- or 3,5,6-trichloro-*p*-cresol, the probability of the formation of these being equal.

3,5-Disulfonic acid was prepared by heating the potassium monosulfonate of *p*-cresol with fuming sulfuric acid[2] on the water bath. The diluted solution was then treated with a current of chlorine to saturation and warmed on the water bath. The oil which formed was collected, washed and crystallized from hot alcohol, yielding white crystals which melted at 39°. It has been identified as 3,5-dichloro-*p*-cresol. The yield obtained from 5 g. of *p*-cresol was 3 g.

Thymol.

By the action of chlorine upon an aqueous solution of a mixture of thymol mono- and disulfonic acids, the sulfonic radicals are detached with the formation of 2,5,6-trichloro-thymol. It has previously been obtained by passing chlorine into thymol.

Four g. of thymol was gradually digested with a mixture of equal volumes of conc. and fuming sulfuric acids and kept on the water bath[3] for about two hours when a clear solution was obtained by the addition of water. A current of chlorine was then passed through the diluted sulfonic acid solution for a long time and a white precipitate obtained. The solid when collected, washed and crystallized from boiling alcohol, yielded 5.7 g. of light brown crystals melting at 61°. It has been identified as 2,5,6-trichloro-thymol.

Carvacrol.

By the action of chlorine upon an aqueous solution of carvacrol-5-sulfonic acid, the sulfonic acid group is detached with the formation of trichloro-carvacrol.

[1] Engelhardt and Latschinow, *Z. Chem.*, 1869, p. 619.

[2] Engelhardt and Latschinow, *Ibid.*, 1869, p. 620.

[3] Engelhardt and Latschinow, *Ibid.*, 1869, p. 46

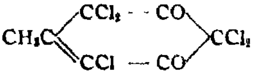
The sulfonic acid is prepared by the action of 5 cc. of conc. sulfuric acid upon 5 cc. of carvacrol[1] on the water bath for an hour. The resulting liquid was then diluted with water and treated with a current of chlorine gas to saturation, the solution gradually becoming turbid. An oil settles which was washed and dried over fused calcium chloride, yielding 3.8 cc. and was found to decompose on boiling at atmospheric pressure. It was shown to be trichloro-carvacrol.

Subs., 0.2980: AgCl, 0.5061.

Calc. for trichloro-carvacrol: Cl, 42.01 Found 42.06

Orcinol.

By the action of chlorine upon an aqueous solution of orcinol-disulfonic acid, the sulfonic groups are detached with the formation of pentachloro-orcinol or 3,5-diketo-methylpentachloro-R-hexane,



It has previously been prepared together with pentachloro-*m*-diketo-R-hexane[2] by the action of excess of chlorine hydrate or potassium chlorate and mineral acid on orcinol.[3]

The disulfonic acid of orcinol was prepared by warming 5 g. of orcinol with 12 cc. (an excess) of conc. sulfuric acid[4] to 60–80° on the water bath for an hour, when the mixture was found to be completely soluble in water. It was diluted with water and treated with chlorine. A precipitate of ash-colored solid substance was immediately obtained, and complete precipitation took place within an hour. The solid when collected, washed and crystallized from glacial acetic acid yielded 8 g. of white crystals, melting at 120.5°. It was identified as pentachloro-orcinol.

o-Nitrophenol.

By the action of chlorine upon an aqueous solution of *o*-nitrophenol-4-sulfonic acid, the sulfonic radical is detached with the production o 4,6-dichloro-*o*-nitrophenol. This substance has previously been prepared by the action of fuming nitric acid upon 2,4-dichlorophenol,[5] and also upon the sulfonic acid of 2,4-dichlorophenol.[6] It has also been produced by leading chlorine in 4-chloro-*o*-nitrophenol.[7]

The sulfonic acid is prepared by the action of 5 cc. of fuming sulfuric acid upon 4 g. of *o*-nitrophenol[8] in the cold to avoid charring. The mixture was left to stand for an hour and then diluted with water and treated with chlorine. Solid accumulated gradually and care was taken to get the maximum yield. The solid was collected, washed and crystallized from glacial acetic acid, yielding 6 g. of yellow crystals, melting at 122–3°. It was identified as 4,6-dichloro-*o*-nitrophenol.

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[1] Claus and Fhrion, *J. prakt. Chem.*, [2] 39, 356 (1889).

[2] Zincke, *Ber.*, 26, 317 (1893).

[3] Stenhouse, *Ann.*, 163, 175 (1872).

[4] Hesse, *Ibid.*, 117, 324 (1861).

[5] Fischer, *Ann. Spl.*, 7, 185 (1870).

[6] Armstrong, *Z. Chem.*, 1871, p. 678.

[7] Faust and Saame, *Ann. Spl.*, 7, 195 (1870).

[8] Kekulé, *Z. Chem.*, 1867, p. 641.

p-Nitrophenol.

By the action of chlorine on an aqueous solution of *p*-nitrophenol-2-sulfonic acid, the sulfonic acid radical is detached with the formation of 2,6-dichloro-*p*-nitrophenol. It has been prepared by leading chlorine through molten *p*-nitrophenol,[1] and by nitrating the dichlorinated *p*-phenol sulfonic acid.[2]

The sulfonic acid is prepared by the gradual addition of 3 cc. of fuming sulfuric acid to 4 g. of *p*-nitrophenol.[3] The mixture was allowed to stand for an hour, dissolved in water and treated with chlorine for some time, when there was a copious precipitation of a yellow substance. The solid was collected, washed, and crystallized from glacial acetic acid and yielding 5 g. of light brown crystals, melting at 125°. The substance was identified as 2,6-dichloro-*p*-nitrophenol.

o-Nitraniline.

By the action of chlorine upon an aqueous solution of *o*-nitraniline sulfonic acid the sulfonic radical is detached with the formation of 4,6-dichloro-*o*-nitraniline. This substance has previously been prepared by nitrating 2,4-dichloro-acetanilide[4] or by chlorinating 4-chloro-2-nitroacetanilide,[5] also by leading chlorine into a solution of *o*-nitraniline dissolved in conc. hydrochloric acid.[6]

Two g. of *o*-nitroaniline and 8 cc. of conc. sulfuric acid were heated to 140–50°, in an oil bath for 8 hours. The solution was allowed to cool and then diluted with water. Chlorine passed through the diluted solution gave at once a copious brown precipitate, complete in about two hours. This precipitate was collected, washed with little water as it is fairly soluble in water. It is freely soluble in glacial acetic acid and can be crystallized from boiling dil. acetic acid, yielding brown crystals which melt at 100°. The nearly theoretical yield of 3.75 g. of pure substance was obtained. It was identified as 4,6-dichloro-*o*-nitroaniline.

p-Nitraniline.

By the action of chlorine gas upon an aqueous solution of *p*-nitroaniline sulfonic acid, the sulfonic acid radical is detached with the formation of

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[1] Schifert, *Ann. Spl.*, 7, 189 (1870).

[2] Armstrong, *Z. Chem.*, 1871, p. 518.

[3] Post, *Ann.*, 205, 38 (1880); Korner, *Jahresb.*, 1872, p. 604.

[4] Witt, *Ber.*, 7, 1603 (1874).

[5] Witt, *Ibid.*, 8, 820 (1875).

[6] Langer, *Ann.*, 215, 111 (1882).

2,6-dichloro-*p*-nitroaniline. It has previously been obtained by the action of chlorine upon *p*-nitroaniline.[1]

Two g. of *p*-nitroaniline and an excess of conc. sulfuric acid were heated in an oil bath to 140–50° for 8 hours. This digested solution was allowed to cool, diluted with water, and treated with chlorine. There was a copious precipitation, complete in about a half hour. The precipitate when collected, washed and crystallized from glacial acetic acid yielded 2.37 g. of yellow crystals melting at 189° which were identified as 2,6-dichloro-*p*-nitroaniline.

m-Nitraniline.

When *m*-nitraniline is sulfonated with excess of conc. sulfuric acid, heated in an oil bath to 140–50° and chlorine passed into the diluted solution a black solid gradually separates. Glacial acetic acid, benzene, ether and alcohol failed to give crystals from this solid. It smelled of chloroquinone and contained mostly tarry substances.

Salicylic Acid.

By the action of chlorine upon an aqueous solution of salicylic sulfonic acid, the sulfonic acid radicals are detached with the formation of 3,5-dichloro-salicylic acid. This has previously been prepared by cautiously heating one molecule of salicylic acid with 3 to 4 molecules of antimony pentachloride.[2] It has also been prepared by the action of chlorine upon an acetic acid solution of salicylic acid[3] and by the action of chlorine upon a cold solution of salicylic acid in potassium hydroxide.[4]

The sulfonic acid derivative was obtained by warming 6 g. of salicylic acid with 10 cc. of conc. sulfuric acid[5] slowly and carefully on the water bath until the mass becomes soluble in water. A current of chlorine was then passed through the solution for a long time. The solid thus obtained was collected, washed and crystallized from glacial acetic acid, giving 8.3 g. of white crystals melting at 215°, which were identified as 3,5-dichloro-salicylic acid.

m-Oxybenzoic Acid.

By the action of chlorine upon an aqueous solution of the trisulfonic-*m*-oxybenzoic acid, the sulfonic radicals are detached with the formation of 2,4,6-trichloro-*m*-oxybenzoic acid. It has previously been prepared by leading chlorine into an acetic acid solution of *m*-oxybenzoic acid.[6]

The sulfonic acid derivative is prepared by gradually treating 10 g. of *m*-oxybenzoic acid at 250° with a mixture of 10 cc. of conc. and 20 cc.

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[1] Korner, *Jahresb.*, 1875, 323, Witt, *Ber.*, 8, 143 (1875).

[2] Lossner, *J. prakt. Chem.*, [2] 13, 429 (1876).

[3] Smith, *Ber.*, 11, 1225 (1878).

[4] Tarugi, *Gazz. chim. ital.*, 30, II, 487 (1900).

[5] Remsen, *Ann.*, 179, 107 (1876).

[6] Zincke, *Ibid.*, 261, 239 (1891).

of fuming sulfuric acid. Five g. of phosphorus pentoxide[1] was then added and the whole was gradually heated on the sand bath to 250° for 8 hours. The mass was then cooled and dissolved in a large volume of water. The solution was filtered from any undissolved substance and treated with chlorine for 12 hours when there was a copious precipitation; care was taken to get the maximum yield. The solid was collected, washed and crystallized from dil. acetic acid, and thus obtained in a yield of 12 g. of white crystals melting at 104–5°. It was identified as 2,4,6-trichloro-*m*-oxybenzoic acid. A small amount of tetrachloroquinone was also formed as a secondary product.

p-Oxybenzoic Acid.

By the action of chlorine upon an aqueous solution of 3-sulfonic-*p*-oxybenzoic acid, the sulfonic radical is replaced with the formation of 3,5-dichloro-*p*-oxybenzoic acid. It has previously been prepared by the action of antimony pentachloride on *p*-oxybenzoic acid.[2] It is also easily obtained by leading chlorine into a 10% acetic acid solution of *m*-oxybenzoic acid.[3]

The sulfonic acid was prepared by treating 7 g. of *p*-oxybenzoic acid with a mixture of 5 cc. of conc. and 5 cc. of fuming sulfuric acids and carefully heating on the sand bath. The mass solidified at first, whereupon another 10 cc. of fuming sulfuric acid was gradually added to it. The heating was continued for 8 hours, when the mass was found to dissolve completely in water. Chlorine was passed into this solution for 8 hours, precipitating a solid substance which was collected, washed and crystallized from glacial acetic acid, yielding 5 g. of a white solid which melted with decomposition at 255–6°. It was identified as 3,5-dichloro-*p*-oxybenzoic acid.

Investigations along similar lines are being continued.

Our thanks are due to Wolcott Gibbs Memorial Fund for a grant defraying part of the expenses of the investigation.

CALCUTTA, INDIA.

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[1] Kretschy, *Ber.*, 11, 858 (1878).

[2] Loessner, *J. prakt. Chem.*, [2] 13, 434 (1876).

[3] Zincke, *Ann.*, 261, 250 (1891).

[CONTRIBUTION FROM THE UNIVERSITY COLLEGE OF SCIENCE OF CALCUTTA.]

REPLACEMENT OF SULFONIC GROUPS BY NITRO GROUPS BY MEANS OF NITROUS GASES.

BY RASIK LAL DATTA AND PHULDEO SAHAYA VARMA.

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The replacement of sulfonic acid groups by nitro groups has not hitherto been studied although a few isolated instances of this sort are to be found in the literature. Thus, Neville and Winther[1] obtained dinitrocresol from *o*-, *m*-, and *p*-cresol sulfonic acids by the action of nitric acid; Werner and Kelbe[2] prepared dinitro-bromothymol from β-bromothymol sulfonic acid, and α-nitro-bromothymol from α-bromothymol sulfonic acid; Michler and Walder[3] obtained mononitro-dimethylaniline from dimethylaniline sulfonic acid by the action of sodium nitrite and sulfuric acid.

It has been found that this replacement can be effected very easily by means of nitrous gases, and that in the course of the reaction more nitro groups frequently enter the molecule with the formation of highly nitrated compounds. In fact, it has been found that those nitrations which hitherto have been achieved only by means of strong nitric acid or by means of nitric-sulfuric acid mixtures, can often be smoothly and easily brought about by the above method. Again many nitrations which cannot be brought about at all by nitric acid can be smoothly accomplished by this method.

This reaction is further useful in elucidating the constitution of nitro bodies derived from known sulfonic acids. The mechanism of the reaction may in all probability be represented thus:

$$R.SO_3OH + \begin{matrix} NO \\ | \\ NO_2 \end{matrix} = R.NO_2 + NOSO_3OH$$

The nitrous gases react upon the sulfonic acid with the formation of the nitro derivative and nitrosyl sulfuric acid. The nitrosyl sulfuric acid in aqueous medium decomposes again into sulfuric acid and nitrous gases which continue further action in the same way.

The replacement of sulfonic group by the nitro group in phenol and cresol sulfonic acids with the formation of 2,4,6-trinitrophenol and trinitrocresol, respectively, has already been described.[4]

The following general behavior can be noted: Aromatic compounds which are already substituted by hydroxyl or halogen radicals have been found to be nitrated readily with the replacement of the sulfonic group. In some cases more nitro-groups enter the ring in suitable positions. In the case of carboxylic acids of hydroxy compounds, not only the sulfonic group but also the carboxyl group is replaced with the formation of nitro-bodies. If the compound does not already contain substituted hydroxyl, and halogen groups, the replacement does not take place at all, as in the case of benzene sulfonic acid which remains unacted upon on treatment with nitrous gases.

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[1] *Ber.*, 13, 1946 (1880).

[2] *Ibid.*, 16, 617 (1883).

[3] *Ibid.*, 14, 2176 (1881).

[4] Datta and Varma, [illegible]

The following detailed results have been obtained: *o*-Cresol-3-sulfonic acid and *o*-cresol-4-sulfonic acid yield 3,4-dinitro-*o*-cresol; *o*-cresol-3,5-disulfonic acid, 3,5-dinitro-*o*-cresol; *m*-cresol-6-sulfonic acid and *m*-cresol-2,6-disulfonic acid, 2,4,6-trinitro-*m*-cresol; *p*-cresol-3-sulfonic acid gives 3,5-dinitro-*p*-cresol; 1,2,4-xylenol gives 3,5-dinitro-1 2,4-xylenol; 1,3,4-xylenol yields 5-nitro-1,3,4-xylenol, 1,4,5-xylenol gives 2-nitro-1,4,5-xylenol; thymol sulfonic acid yields 6-nitrothymol; resorcinol disulfonic acid yields 2,4,6-trinitro-resorcinol; anisol and phenetol sulfonic acids give 2,4-dinitrophenol, the alkyloxyl group being hydrolyzed in both the cases; *o*-nitrophenol-4-sulfonic acid, *m*-nitrophenol sulfonic acid and *p*-nitrophenol sulfonic acid give 2,4,6-trinitrophenol. *o*-Oxybenzoic acid and *p*-oxybenzoic acid yield 2,4,6-trinitrophenol, whereas *m*-oxybenzoic acid yields 2,4,6-trinitro-resorcinol; 3,5-dinitro-*o*-cresol can be obtained from *o*-cresotonic acid (1 : 2 : 3); 2,4,6-trinitro-*m*-cresol from *m*-cresotonic acid (1 : 3 : 4); and 3,5-dinitro-*p*-cresol from *p*-cresotonic acid (1 : 4 : 3). Sulfonic acids of chlorobenzene, bromobenzene and iodobenzene yield *p*-chloronitrobenzene, *p*-bromonitrobenzene and *p*-iodonitrobenzene, respectively. *o*-Iodotoluene gives *p*-nitro-*o*-iodotoluene. Benzyl cyanide has been found to give *p*-nitrobenzyl cyanide. Anthraquinone-β-sulfonic acid yields β-nitro-anthraquinone.

These interactions are generally effected in aqueous solutions, with the passage of nitrous gases to saturation. Finally the nitro compounds are crystallized from the solution.

Experimental.

o-Cresol. Preparation of 3,4-Dinitro-*o*-cresol and 3,5-Dinitro-*o*-cresol.

_o_-Cresol-3-sulfonic acid was prepared according to the method described by Claus and Jackson.[1] The crude product after sulfonation was distilled in steam to free it from unchanged *o*-cresol. To the diluted solution of *o*-cresol-3-sulfonic acid nitrous gases were added until absorption was complete. The solution was evaporated until crystals appeared and cooled, when the greater part of it crystallized. The crystals were drained, washed with a small quantity of water and finally recrystallized from absolute alcohol when they melted sharply at 89.5°. As this melting point did not correspond with that of any known nitro-compound of *o*-cresol the substance was analyzed and was found to be a dinitro-*o*-cresol:

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[1] *J. prakt. Chem.*, [2] 38, 333 (1888).

Subs., 0.1011: 13.4 cc. N_2 at 29° and 745.5 mm.
Calc. for $C_6H_3.CH_3(OH)(NO_2)_2$: N, 14.14. Found: 14.70.

o-Cresol-4-sulfonic acid was prepared by digesting equimolecular quantities of *o*-cresol and strong sulfuric acid.[1] On treating this with nitrous gases as before the same dinitro-compound melting at 89.5° was obtained. Since this dinitro-compound is obtained both from *o*-cresol-3-sulfonic acid and *o*-cresol-4-sulfonic acid, the substance obtained is evidently 3,4-dinitro-*o*-cresol.

o-Cresol-3,5-disulfonic acid was prepared by dissolving *o*-cresol in fuming sulfuric acid and warming the mixture for some time on the water bath.[2] The crude mixture was distilled in steam to free it from unchanged cresol which otherwise chars under the influence of nitrous gases, diminishing the yield and giving an impure product. The resulting solution was saturated with nitrous gases and evaporated on the water bath until crystals separated. These were recrystallized from alcohol and then melted at 85°. This substance was identified as 3,5-dinitro-*o*-cresol. The yield was about 70% of the theoretical amount.

m-Cresol. Preparation of 2,4,6-Trinitro-*m*-cresol.

m-Cresol-6-sulfonic acid was prepared by mixing equimolecular quantities of *m*-cresol and strong sulfuric acid according to the method of Claus and Kraus.[3] The resulting product was distilled in steam to get rid of unchanged *m*-cresol. After saturating with nitrous gases and evaporating, crystals were obtained. These on recrystallization from alcohol gave pure 2,4,6-trinitro-*m*-cresol, melting at 109–10° which was further identified by analysis:

Subs., 0.1103: 17.7 cc. N_2 (28° and 746 mm.).
Calc. for $C_6H(CH_3)(NO_2)_3OH$: N = 17.30. Found: 17.70.

The yield of trinitro-*m*-cresol was about 50% of the theoretical amount.

m-Cresol-2,6-disulfonic acid was prepared from one part of *m*-cresol and 6 parts of strong sulfuric acid, warmed for about 6 hours at 120–60°.[4] The product was purified from unchanged *m*-cresol and saturated with nitrous gases. On evaporating and cooling, crystals of 2,4,6-trinitro-*m*-cresol were obtained which on crystallization from alcohol melted at 109–10°.

p-Cresol. Preparation of 3,5-Dinitro-*p*-cresol.

p-Cresol-3-sulfonic acid was prepared by adding fuming sulfuric acid gradually to *p*-cresol, the vessel containing the mixture being cooled from time to time in cold water and the mixture all along shaken vigorously. It was distilled in steam in the usual manner to free it from unchanged cresol. On passing nitrous gases, a precipitate began to form, the quantity increasing with the passing of the gas. During the absorption of the gas much heat was developed and it was necessary to keep the mixture cold by immersing the vessel in cold water. The product was collected and recrystallized from absolute alcohol when it melted at 84°, and was identified as 3,5-dinitro-*p*-cresol. If the passing of the nitrous gases be continued for a sufficiently long time, much oxalic acid is formed as a result of destructive oxidation.

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[1] Engelhardt and Latschinow, *Z. Chem.*, 1869, p. 620; Haulke, *Ber.*, 20, 340 (1887).

[2] Claus and Jackson, *Loc. cit.*

[3] *Ber.*, 20, 3089 (1887).

[4] Claus and Kraus, *Loc. cit.*

1,2,4-Xylenol. Preparation of 3,5-Dinitro-1,2,4-xylenol.

1,2,4-Xylenol sulfonic acid was prepared by heating on the water bath for about $^1/_2$ hour 10 g. of xylenol and 20 cc. of conc. sulfuric acid. The product was then diluted with water and treated with nitrous gases. The solution turned dark in color at once and a black, resinous mass was deposited on the surface, some dark-colored thick liquid settling at the bottom of the vessel. A considerable quantity of heat was developed. The passing of the nitrous gases was continued for nearly an hour when the black, resinous mass and the separated oil were transformed gradually into a yellow solid product which on crystallization from alcohol gave bright yellow crystals melting at 125–6° and identified as 3,5-dinitro-1,2,4-xylenol. The yield was nearly quantitative.

1,3,4-Xylenol. Preparation of 5-Nitro-1,3,4-xylenol.

1,3,4-Xylenol sulfonic acid was obtained by heating on the water bath for 2 to 3 hours 10 cc. of the xylenol with 25 cc. of a mixture of equal quantities of fuming and conc. sulfuric acids. The mixture was distilled in steam to free it from unchanged xylenol, diluted with water and then treated with nitrous gases. The solution began to turn turbid and the color changed from dark to yellow, clearing in 30 to 40 minutes, when a considerable quantity of yellow solid product collected on the surface of the liquid. This solid, crystallized from alcohol, gave beautiful crystals melting at 72°, which were identified as 5-nitro-1,3,4-xylenol.

1,4,5-Xylenol. Preparation of 2-Nitro-1,4,5-xylenol.

1,4,5-Xylenol was sulfonated by mixing 10 g. of xylenol and 20 cc. of conc. sulfuric acid and heating on the water bath for about an hour. The product was diluted with water and treated with nitrous gases. The solution was at first dark green in color, an emulsion-like product being formed; but after some time the solution became clear with the separation of a yellow, solid product which on crystallization from benzene yielded light yellow crystals melting at 116–7°, identified as 2-nitro-1,4,5-xylenol. The yield was quantitative.

Thymol. Preparation of 6-Nitrothymol.

Thymol sulfonic acid was prepared by heating thymol with fuming sulfuric acid at 160–80° on a paraffin bath for about two hours and a half.[1] A dark-colored, viscid mass was obtained. This was mixed with a small quantity of water and allowed to stand, when it solidified on cooling. The solid was removed and purified by suction. The product was dissolved in water and the treatment with nitrous gases continued for 3 hours since the reaction is very sluggish. The solution was evaporated on the water bath when an oil separated which solidified on cooling. This, when recrystallized from alcohol, melted at 130° and was identified as 6-nitrothymol. The mother liquor, after the separation of crystals, gave a small yield of oxalic acid due to exhaustive oxidation.

Resorcinol. Preparation of 2,4,6-Trinitro-resorcinol.

Resorcinol disulfonic acid was prepared by adding one part of resorcinol to about two parts of fuming sulfuric acid and heating on the water bath for about an hour.[2] The dark-colored product after diluting with water was treated with nitrous gases when the color cleared to yellow at the end of the reaction. On evaporating on the water bath crystals were obtained which on recrystallization from alcohol gave fine, yellow crystals, melting at 175–6°. This was identified as 2,4,6-trinitro-resorcinol. The yield was good.

Anisol. Formation of 2,4-Dinitrophenol.

Equal volumes of anisol and sulfuric acid were thoroughly mixed and heated on the water bath for about an hour. The liquid obtained was then diluted with water and nitrous gases were passed into it for about an hour and a half. The resulting solution was concentrated on the water bath until on cooling the liquid partly solidified. The substance was separated and recrystallized from alcohol when it melted sharply at 115°. It was identified as 2,4-dinitro-phenol.

Subs., 0.1216: 17.4 cc N_2 (30° and 760 mm.).
Calc for $C_6H_3(NO_2)_2OH$. N = 15.22. Found: 15.92.

Besides the usual replacement and nitration, the methoxyl group is here hydrolyzed to hydroxyl under the influence of nitrous gases.

Phenetol. Formation of 2,4-Dinitrophenol.

Equal volumes of phenetol and sulfuric acid were heated on the water bath, and the product mixed with water and treated with nitrous gases. The resulting solution on concentration partially solidified. The solid was collected and recrystallized from alcohol when it melted at 115–6° and was identified as 2,4-dinitrophenol. The reaction here is strictly analogous to the one with anisol.

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[1] Engelhardt and Latschinow, *Z. Chem.*, 1869, p. 44. Lieberman (*Ber.*, 10, 612 (1817)) prepared 6-nitrothymol by the action of nitric acid on an aqueous solution of the corresponding sulfonic acid.

[2] Tideschi, *Ber.*, 21, 1267 (1888).

o-Nitrophenol. Formation of 2,4,6-Trinitrophenol.

***o*-Nitrophenol** was sulfonated by adding in small quantities at a time one and a half molecular weight of comparatively weak fuming sulfuric acid to one molecular weight of the substance. During the addition of the acid much heat was evolved and the vessel was cooled from time to time to prevent any loss by charring and other side reactions. When the addition of the acid was complete, the mixture was heated for nearly an hour on the water bath. It was diluted with water, filtered to separate the few black particles present and treated with nitrous fumes. The solution obtained after sulfonating the nitrophenol was yellow in color. During the passage of the gases very little change in color of the solution took place. The solution was then evaporated on a water bath till a solid incrustation had formed On cooling, more solid precipitate was obtained. This was separated, dried and recrystallized from alcohol. It was identified as 2,4,6-trinitrophenol. The theoretical yield was obtained.

m-Nitrophenol. Formation of 2,4,6-Trinitro-resorcinol.

***m*-Nitrophenol** was sulfonated by mixing one molecular weight of nitrophenol with one and a half molecular weights of fuming sulfuric acid the latter being added drop by drop. During the addition, the mixture was kept cooled by cold water. When the whole of the acid had been added, the mixture was heated on the water bath for half an hour. It was diluted with water, filtered from the few black particles present, and then submitted to the action of nitrous gases for nearly two hours. The solution, originally dark in color, changed gradually to pale yellow, and when the action was complete, was evaporated on the water bath until a crust formed on the surface. More solid was obtained on cooling which was separated by filtration, dried and crystallized from absolute alcohol, when it melted sharply at 174–5° and was found to be trinitro-resorcinol. The yield was quantitative.

p-Nitrophenol. Formation of 2,4,6-Trinitrophenol.

***p*-Nitrophenol** was dissolved in a little more than the equimolecular quantity of fuming sulfuric acid and the mixture heated on the water bath for about half an hour. The product was dissolved in water and the undissolved solid particles were removed by filtration. The solution thus obtained was dark-colored and was, therefore, treated with animal charcoal. Nitrous gases were passed through the filtrate for about 45 minutes and were readily absorbed, the color changing from dark to greenish yellow and finally yellow. The solution was concentrated on the water bath and allowed to cool, when solid crystals were obtained which melted at 122° after recrystallization from alcohol. This substance has been identified as 2.4.6-trinitrophenol. The yield was good.

o-Oxybenzoic Acid. Formation of 2,4,6-Trinitrophenol.

Salicylic acid was dissolved in conc. sulfuric acid (one molecular weight of the former with one and a half molecular weights of the latter) and the mixture heated on the water bath for nearly one hour. The solution thus obtained was diluted with water to 3 times its volume and nitrous fumes were passed into it for nearly two hours. The dark-colored solution changed gradually to yellow. During the passage of the fumes through the solution there was considerable evolution of carbon dioxide. The solution obtained was concentrated by heating on the water bath and cooling, giving beautiful, yellow crystals which proved on drying and crystallizing from alcohol to be 2,4,6-trinitrophenol, melting at 122.5°. A quantitative yield was obtained.

m-Oxybenzoic Acid. Formation of 2,4,6-Trinitro-resorcinol.

m-Oxybenzoic acid does not appear to form a sulfonic acid very easily with conc. sulfuric acid. The oxybenzoic acid was dissolved in fuming sulfuric acid and the mixture heated on a water bath for nearly 3 hours. The dark-colored liquid thus obtained was diluted with water and treated with nitrous fumes until no more heat was evolved and the formation of gas in the solution had practically ceased. The solution was then concentrated until a crust formed. It was then cooled when a large quantity of yellow product was obtained, which on separation and crystallization was identified as 2,4,6-trinitro-resorcinol, melting at 175.5°. The yield was good

p-Oxybenzoic Acid. Formation of 2,4,6-Trinitrophenol.

A mixture of 10 g. of *p*-oxybenzoic acid dissolved in 20 cc. of fuming sulfuric acid was heated on a water bath for about two hours and a half. The product was dissolved in water and treated with nitrous gases until no more heat was evolved. Gas was evolved from solution, and at a certain stage the evolution was so rapid as to give the appearance of brisk boiling. During this period the color of the solution changed from dark to greenish and finally yellowish green. In about an hour and a half the operation was stopped and the solution concentrated till a solid incrustation formed on the surface of the liquid. On cooling, crystals separated which on recrystallization from water melted at 122.5° and were identified as 2,4,6-trinitrophenol. The yield was quantitative.

o-Cresotonic Acid (1:2:3). Formation of 3,5-Dinitro-*o*-cresol.

A mixture of 10 g. of *o*-cresotonic acid with 30 cc. of fuming sulfuric acid was thoroughly shaken and heated on a water bath for about one hour and a half. The dark-colored liquid thus obtained was dissolved in water very carefully by adding small quantities to cold water. Nitrous gases were then passed through this dark-colored solution when gas evolution set up gradually and in less than turbid and a yellow precipitate began to form. In an additional half hour the precipitation was found to be complete, leaving a clear solution. The solid was dried and recrystallized from alcohol when it melted at 85–6° and was identified as 3,5-dinitro-*o*-cresol. The yield was quantitative.

m-Cresotonic Acid (1:3:4). Formation of 2,4,6-Trinitro-*m*-cresol.

The sulfonic acid derivative of this substance was prepared by dissolving 10 g. of *m*-cresotonic acid in 20 cc. of fuming sulfuric acid and heating the mixture on a water bath for one hour and a half only. The dark-colored liquid was added drop by drop to cold water and the resulting solution submitted to the action of nitrous gases, when as in the case of *o*-cresotonic acid, effervescence commenced, heat was evolved, and the solution became turbid. In an additional half hour the formation of the yellow precipitate was complete, the passing of the gases being continued until no more heat evolution could be noticed. The product was concentrated on the water bath when the precipitate dissolved, but it reprecipitated in copious quantity on cooling. It was filtered and crystallized from alcohol 3 times when it melted sharply at 109–10°, and was identified as 2,4,6-trinitro-*m*-cresol.

p-Cresotonic Acid (1:4:3). Formation of 3,5-Dinitro-*p*-cresol.

By the action of nitrous fumes on the sulfonic acid derivative of *p*-cresotonic acid, 3,5-dinitro-*p*-cresol was obtained in theoretical yield in a high state of purity. The sulfonic acid derivative consists of colorless, fine, needle-shaped crystals not quite so easily soluble as the sulfonic acid derivatives of the other cresotonic acids. It was prepared by dissolving 10 g. of the *p*-cresotonic acid in 20 cc. of fuming sulfuric acid and heating the mixture for nearly two hours on a water bath. When the action was complete the product was mixed with water and at once solidified to a mass of fine crystals, which were dissolved in water and submitted to the action of nitrous fumes. A solid formed on the surface of the liquid with the liberation of much heat and the evolution of minute bubbles of gas. When no sign of further reaction could be noticed, the operation was stopped and the solid separated, dried on a porous plate and crystallized from alcohol. The mother liquor was concentrated on the water bath and more solid obtained on cooling. These beautiful, yellow crystals proved to be 3,5-dinitro-*p*-cresol, melting at 84°.

Chlorobenzene. Preparation of *p*-Nitrochlorobenzene.

Equal volumes of chlorobenzene and strong sulfuric acid were mixed and heated on the water bath for about two hours. Nitrous fumes were then bubbled through the solution for nearly two hours after which no more action between the substances could be noticed. The action in this case was slower than in the case of iodo and bromobenzene sulfonic acids.

No solid appeared in this case, but by pouring the liquid in cold water, a solid separated from solution. It was filtered off, dried and recrystallized from alcohol, when it melted sharply at 82–3°, and has been identified as *p*-nitrochlorobenzene.

Bromobenzene. Preparation of *p*-Nitrobromobenzene.

Equal volumes of bromobenzene and fuming sulfuric acid were mixed and heated on the water bath for about an hour. The solution was then slightly diluted with water and treated with nitrous gases for half an hour, when crystals began to form on the sides of the vessel. The solution was shaken from time to time and to prevent too much rise of temperature, the vessel was cooled by immersing in cold water. When the action slackened, the liquid was poured into a large volume of water whereupon the solid product precipitated. The whole operation did not take more than an hour. The solid on crystallization from glacial acetic acid proved to be *p*-nitrobromobenzene, melting at 116–27°.

Iodobenzene. Preparation of *p*-Nitroiodobenzene.

Iodobenzene sulfonic acid was prepared by shaking thoroughly equal volumes of iodobenzene and fuming sulfuric acid and heating the mixture on a water bath for an hour. It was cooled and then submitted to the action of nitrous gases. In a few minutes a copious precipitate formed, to which water was added to effect a complete separation of the solid. The latter was separated by decantation, dried on a porous plate and crystallized from benzene. It melted sharply at 170–1° and was identified as *p*-nitroiodobenzene.

o-Iodotoluene. Preparation of *p*-Nitro-*o*-iodotoluene.

o-Iodotoluene was mixed with twice its volume of fuming sulfuric acid and heated for 4 hours, when the reaction seemed to be complete. It was then diluted with water and submitted to the action of nitrous fumes for 2 to 3 hours. The action was comparatively slow, and when no more heat was evolved the current of nitrous gases was discontinued, the mixture shaken thoroughly and poured into a large volume of water, when a solid product was obtained which on repeated crystallization melted at 102°. It was identified as *p*-nitro-*o*-iodotoluene. The yield was good although not quantitative, due probably to the incomplete formation of the sulfonic acid.

Benzyl Cyanide. Preparation of *p*-Nitrobenzylcyanide.

By the action of nitrous gases on benzyl cyanide dissolved in strong sulfuric acid, *p*-nitrobenzylcyanide was obtained. This compound has been previously obtained by the action of 5 parts of nitric acid on one part of benzyl cyanide.

A mixture of 10 cc. of strong sulfuric acid and 10 cc. of benzyl cyanide was well shaken for about 15 minutes and then heated on a water bath for an hour. The action was very vigorous at first and the solution became a dark-colored, viscous mass. This was dissolved in water and treated with nitrous gases, when much heat was evolved with the formation of a dark, oily product. This oil was separated and allowed to stand until the change into a yellow product was complete. On recrystallization from acetic acid the substance melted at 83°, and was identified as *p*-nitrobenzylcyanide.

Anthraquinone. Preparation of β-Nitro-anthraquinone.

A mixture of 10 g. of anthraquinone and 10 cc. of fuming sulfuric acid was heated on a paraffin bath for about 2 hours, and the product dissolved in water and treated with nitrous gases. When reaction was complete, the solution was evaporated and a yellow solid obtained. It was soluble in chloroform and acetone, from which on crystallization a product melting at 180° was obtained, which was identified as β-nitro-anthraquinone.

Additional investigations along similar lines are being made.

CALCUTTA, INDIA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA]

TETRAPHENYLDIARSINE.

BY C. W PORTER AND PARRY BORGSTROM

Received September 6, 1919.

The earliest attempt to prepare tetraphenyldiarsine was made by LaCoste and Michaelis[1] who heated diphenylchloroarsine, $(C_6H_5)_2AsCl$, with zinc in a sealed tube at 100°. The crystalline body they obtained melted at 154°, and analyses showed 53.01% carbon instead of 62.88%, the theoretical value. Lack of material prevented them from making further examination of this body.

Two years later Michaelis and C. Schulte[2] reported the preparation of tetraphenyldiarsine by heating tetraphenyldiarsine oxide, $(C_6H_5)_4As_2O$, in absolute ethyl alcohol with phosphorous acid. It was found to be a crystalline body, melting at 135°. The substance oxidized readily in the air forming the anhydride of diphenyl arsenic acid, $(C_6H_5)_4As_2O_3$.

Later, Michaelis[3] reported its preparation by heating an alcoholic solution of diphenylarsenic acid, $(C_6H_5)_2AsOOH$, for 10 hours with a large excess of phosphorous acid. It was described as a crystalline body spontaneously combustible in air. The oxidation product of the substance in a stream of carbon dioxide containing some oxygen was identified as tetraphenyldiarsine oxide.

More important work was done by Schlenk[4] who determined the molecular weight of tetraphenyldiarsine. On the basis of one measurement he concluded that the body does not dissociate at the boiling point of benzene.

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[1] *Ann.*, **201**, 222 (1880)

[2] *Ber.*, **15**, 1952 (1882)

[3] *Ann.*, **321**, 148 (1902)

[4] *Ibid.*, **394**, 216 (1912)

In view of the fact that some aromatic derivatives of ethane[1] and of hydrazine[2] dissociate with the production of free radicals capable of independent existence, it was considered worth while to redetermine the molecular weight of tetraphenyldiarsine and to measure its iodine and oxygen absorption with the hope of securing evidence of dissociation into radicals of the type $(C_6H_5)_2As^-$.

The tetraphenyldiarsine was prepared by means of the following reactions: triphenyl arsine was made from phenylmagnesium bromide and arsenic trichloride.[3] This application of the Grignard reaction was found to be very much more successful than the use of sodium on a mixture of arsenic trichloride and chlorobenzene.[4]

Triphenyl arsine (0.2 mol) and arsenic trichloride (0.1 mol) were heated in sealed tubes to 200° for 4 hours.[5] The mixture of diphenylchloroarsine (b. p. 333°) and monophenyldichloroarsine (b. p. 252°) formed was separated into two components by fractional distillation. The monophenyl derivative was then converted into diphenylchloroarsine by the use of mercury biphenyl.[6]

After complete purification of the substance according to the method of Michaelis[7] it was converted into tetraphenylarsine oxide by boiling with a solution of sodium hydroxide.[7] The oxide was extracted from the solution by ether and recrystallized.

Five g. of the oxide was added to 75 cc. of absolute alcohol. 7.5 g. of solid phosphorous acid was added to 75 cc. of absolute alcohol. Both solutions were saturated with dry nitrogen purified from oxygen according to the method of C. Van Brunt.[8] The solutions were mixed in the apparatus shown in drawing (Fig. 1) after it had been filled with nitrogen and thoroughly dried. The solution was boiled for 3 hours. On cool-

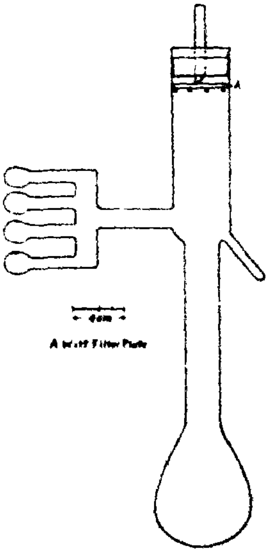

Fig. 1.

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[1] Gomberg, THIS JOURNAL, 22, 757 (1900), and many later papers.

[2] Weiland, *Ann.*, 381, 200 (1911); 392, 127 (1912).

[3] Pfeiffer, *Ber.*, 37, 4620 (1904).

[4] Phillips, *Ibid.*, 19, 1031 (1886).

[5] Michaelis and Paetow, *Ann.*, 233, 64 (1886).

[6] Michaelis and Link, *Ibid.*, 207, 195 (1881).

[7] Michaelis, *Ibid.*, 321, 141 (1902).

[8] THIS JOURNAL, 36, 1448 (1914)

ing, the tetraphenyldiarsine separated as white leaflets. After the mother liquor had been decanted off the crystals were washed by decantation with absolute alcohol and then with dry ether. During the whole process dry nitrogen was passed through the apparatus. The crystals were dried by a stream of warm dry nitrogen and then deposited in the small side tubes by shaking. These were then sealed off without coming in contact with the air.

Pure. dry tetraphenyldiarsine, when exposed to the air, absorbed oxygen. If the crystals were scattered they oxidized in the air without melting, but if in large groups they melted. But the material never became spontaneously inflammable as reported by Michaelis.[1] From the solid oxidation products diphenylarsenic acid, $(C_6H_5)_2AsOOH$ (m. p. 170°) and tetraphenyldiarsine oxide, $(C_6H_5)_4As_2O$ (m. p. 91°) were isolated.

In solution in xylene it showed no color even when heated to 155° in a sealed tube. It was not very soluble in benzene, and at 20° the greatest concentration that could be obtained was about 1%.

Tetraphenyldiarsine reacted with hot alcohol. Fine, needle-shaped crystals were precipitated and the solution became yellowish in color. On evaporation, a yellow oil, with an intense and disagreeable odor, separated. This yellow oil reacted with iodine rapidly and at the same time the solution became acid. On addition of a solution of silver nitrate a yellow precipitate formed which darkened in the light. The compound was identified as diphenylarsine $(C_6H_5)_2AsH$. It had the properties described by Dehn and Wilcox.[2] When oxidized by the air tetraphenyldiarsine was dissolved in dry benzene and allowed to stand with oxygen over it, the absorption of the oxygen slowly approached the quantity necessary for the formation of tetraphenyldiarsine oxide.

A small tube containing tetraphenyldiarsine was broken in absolute benzene which was thoroughly saturated with nitrogen, and at all times there was nitrogen over the solution. The solution absorbed iodine readily and acquired a faint yellow color. This point was noted in each run, but it was not a fixed point. When the solution was older the color appeared with less iodine. The titration with iodine was carried beyond the end-point and the solution allowed to stand. After about 24 hours a crystalline body began to separate from solution. In one run there was a separation of a red oil, but this on standing gradually crystallized. The crude crystals, probably diphenyliodoarsine were brown in color and melted at about 30°.

A tube of tetraphenyldiarsine was broken in an evacuated vessel of one liter capacity. On heating to 200° in an oil bath the vapor pressure developed was about 1 mm. On cooling there was no sign of decomposition, and tetraphenyldiarsine crystallized again. On heating to about 300° there was decomposition, and metallic arsenic was deposited on the sides of the container. The container was opened, the contents extracted and recrystallized. The product melted at 59°, corresponding to triphenylarsine. The decomposition may be represented as follows:

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[1] *Loc. cit.*

[2] *Am. Chem. J.*, 35, 45 (1906).

$$3(C_6H_5)_4As_2 = 4(C_6H_5)_3As + 2As.$$

It was impossible, therefore, to determine the molecular weight of the compound in the vapor phase.

The molecular weight was determined in naphthalene as a solvent. (K = 6900.)

			M. W.	
Wt of substance. G.	Wt of solvent G	Δt	Found	Calc for $(C_6H_5)_4As_2$.
0 4088	41 6	0 090°	755	458
0 6389	45 5	0 126°	765	..

Evidently the tetraphenyldiarsine in naphthalene at the freezing point was not dissociated but rather associated.

Conclusion.

Tetraphenyldiarsine, when exposed to air, oxidized to tetraphenyldiarsine oxide and diphenylarsenic acid. In benzene solution it gradually absorbs oxygen sufficient for the formation of tetraphenyldiarsine oxide. The tetraphenyldiarsine absorbs iodine rapidly, and from the solution a crystalline iodide slowly precipitates. It decomposes in hot alcohol, forming diphenylarsine.

Its vapor pressure at 200° is about 1 mm. At 300° it decomposes in a vacuum with the deposition of arsenic and formation of triphenylarsine.

The molecular weight cannot be determined in the vapor phase due to decomposition. In naphthalene it is apparently associated.

The bond between the arsenic atoms is easily broken, oxygen and iodine being rapidly absorbed; but these experiments furnish no evidence of the independent existence of a bivalent arsenic radical.

BERKELEY, CAL.

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF COLUMBIA UNIVERSITY.
No. 327.]

RESEARCHES ON QUINAZOLINES. XXXIV. THE SYNTHESIS OF CERTAIN NITRO AND AMINO BENZOYLENE UREAS AND SOME COMPOUNDS RELATED THERETO.

BY MARSTON TAYLOR BOGERT AND GEORGE SCATCHARD[1]

Received September 15, 1919.

Introductory.

In 1916, the authors published a paper[2] on dinitro-benzoylene urea, calling attention to the fact that its monosodium salt was a very sensitive indicator for hydrogen ion concentrations between the limits of 6 and 8 on the Sörensen scale.

The experimental work set forth in the present paper supplements that given in the article just mentioned, describes the various steps leading up to the synthesis of the dinitro-benzoylene urea, and records the preparation and study of some related compounds.

Briefly, the work followed these main lines:

1. Anthranilic acid was converted into *o*-uramino benzoic acid by the action of potassium isocyanate in acid solution, the uramino acid changed to benzoylene urea by treatment with conc. sodium hydroxide solution, and the benzoylene urea then nitrated and the nitro derivative reduced.

By direct methylation of benzoylene urea with methyl iodide and alkali, 3-monomethyl and 1,3-dimethyl-benzoylene urea were prepared.

2. *o*-Uramino benzoic acid was nitrated to the dinitro derivative and the latter converted into its methyl ester. By heating the latter with ammonia under pressure, 6-nitro-benzoylene urea was obtained.

3. 5-Nitro-2-acetamino toluene was oxidized to 5-nitro-acetanthranilic acid, the product de-acetylated and fused with formamide, yielding thus the 6-nitro-4-quinazolone.

By direct nitration of benzoylene urea, both mono- and dinitro derivatives were obtained. The second nitro group enters the molecule much more readily than the first In fact, even with calculated (one mole) quantities of nitric acid, it was found difficult to get the mononitro derivative without simultaneous formation of some dinitro.

The structure of the dinitro benzoylene urea is a problem of unusual interest because of the use of its monosodium salt for the purpose mentioned above. The location of one nitro group is quite certainly at position 6, in view of the synthesis of the dinitro derivative from 6-nitro benzoylene urea. It seems most likely that the other nitro group is in position 8, as this would be the natural place for a second one to enter, *meta* to the first nitro group and to the carbonyl group, and *ortho* to the amine group. The ease with which it enters argues against any other location in the benzene side of the nucleus. Attachment to the nitrogens of the miazine half is improbable, because of the formation of the dinitro compound in acid solution (conditions which generally hydrolyze the -N.NO_2 grouping) and of the fact that no nitrogen could be split off from it by boiling with water or with acetic acid. Synthetic proof of this conclusion is still lacking. Since 5-nitro-anthranilic acid refused to react with urea or potassium isocyanate, it seemed useless to attempt the condensation with 3,5-dinitro-anthranilic acid.

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[1] This paper is based upon experimental work carried out by Mr. Scatchard as part of the requirements for the degree of Doctor of Philosophy under the Faculty of Pure Science, Columbia University. Its publication has been delayed by the war service of both authors. M. T. BOGERT.

[2] THIS JOURNAL, 38, 1606 (1916).

Certain of the properties of benzoylene urea merit mention. Like its 7-methyl derivative[1] it forms a dinitro derivative with the greatest ease. This is probably due, in part at least, to its diphenolic character (in the enol form). While benzoylene urea itself readily yields 1- and 3-monomethyl and 1,3-dimethyl derivatives when treated with methyl iodide and a base, dinitro benzoylene urea cannot be methylated at all in the same manner. Connected with this is the fact that neither 3-methyl- nor 1,3-dimethyl-benzoylene urea can be nitrated by long boiling with conc. sulfuric and fuming nitric acids, according to our experiments.

The work of Griess[2] on *o*-uraminobenzoic acid and on its dinitro derivative was repeated and the methyl esters also of these two acids were prepared and studied. The dinitro acid probably has the following constitution: $(2)\text{O}_2\text{N.NH.CO.NH.C}_6\text{H}_3(\text{NO}_2)(5)\text{COOH}(1)$, since when boiled with water it breaks down into 5-nitro-anthranilic acid, nitrous oxide and carbon dioxide. The formation of nitrous oxide indicates that the second nitro group is on the terminal nitrogen of the urea residue, inasmuch as the two nitrogens are found united in the decomposition product. The reaction may be assumed to be a preliminary hydrolysis to nitro-isatoic acid and nitramide, both of which undergo further hydrolysis in the hot aqueous solution, the former into 5-nitro-anthranilic acid and carbon dioxide, the latter into nitrous oxide and water.

$$\text{O}_2\text{N.NH.CO.NH.C}_6\text{H}_3(\text{NO}_2)\text{COOH} + \text{H}_2\text{O} \longrightarrow$$
$$\text{HOOC.NH.C}_6\text{H}_3(\text{NO}_2)\text{COOH} + \text{O}_2\text{N.NH} \longrightarrow$$
$$\text{H}_2\text{N.C}_6\text{H}_3(\text{NO}_2)\text{COOH} + \text{CO}_2 + \text{N}_2\text{O} + \text{H}_2\text{O}.$$

The methyl ester of the dinitro acid decomposes similarly, giving methyl-nitro-anthranilate.

If the action of ammonia followed the same course as with the *meta* acid,[3] breaking out only the nitro group from the side chain and forming

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[1] Niementowski, *J. prakt. Chem.*, [2] 51, 564 (1895).

[2] *J. prakt. Chem.*, [2] 5, 369 (1872).

[3] Griess, *Ibid.*, [2] 5, 227 (1872).

5-nitro-2-uramino-benzoic acid, the latter should condense in the alkaline solution to 6-nitro-benzoylene urea. This reaction could not be realized with the free dinitro acid, for the apparent reason that its instability and velocity of decomposition were too great. The condensation was accomplished, however, with the methyl ester of this acid.

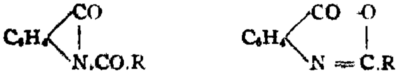
This is in line with the behavior of *o*-uramino-benzoic acid itself, which decomposes when boiled with water, whereas its methyl ester under similar conditions condenses smoothly to benzoylene urea.

The literature of 5-nitro-anthranilic acid was found to be rather badly confused and we hope that we have cleared it up somewhat.

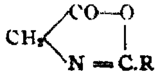
Apparently the nitro group in 5-nitro-anthranilic acid exerts a decided steric hindrance to the replacement of the amino hydrogens by other groups or residues, for it was found impossible to obtain any condensation with urea, or with potassium isocyanate in acid solution, although the attempts were made under various conditions, including the method of Bailey and Read.[1] The method of Sonn[2] for the preparation of substituted ureas was not tried, since Sonn found that the amino groups of anthranilic acid and of *o*-nitraniline were too weakly basic to give the condensation.

Johnson and Scott[3] noted that anthranilic acid refused to condense to a thioquinazolone when treated with ammonium thiocyanate and acetic anhydride. We can corroborate this, and can report that the 5-nitro-anthranilic acid behaves similarly.

If Johnson's theory[4] of the mechanism of this reaction is correct, the above facts are most simply explained on the assumption of a lactame structure for the intermediate acetanthranil, as the latter is the first product of the action of acetic anhydride upon anthranilic acid. If the anthranil[5] possessed the metoxazone structure, it would resemble the lactone anhydrides of the α-amino acids, which are the intermediate products in the formation of thiohydantoins, and should react, therefore, analogously to form a thiobenzoylene urea.


Acylanthranil

(Lactame.) (Metoxazone.)


Lactone anhydride of α-amino acid

By fusion of the 5-nitro-anthranilic acid with formamide, 6-nitro-4-quinazolone was obtained and shown to be identical with the compound prepared by Bogert and Geiger[6] by direct nitration of 4-quinazolone. At the time, Bogert and Geiger expressed the opinion that the nitro group would be found to be in position 6, and this synthesis proves the correctness of the deduction.

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[1] This Journal, 37, 1884 (1915).

[2] *Ber.*, 47, 2437 (1914).

[3] This Journal, 35, 1130 (1913).

[4] *Ibid.*, 35, 1136 (1913).

[5] For a discussion of the structure of acylanthranils, see Heller, *Ber.*, 48, 1183 (1915).

[6] This Journal, 34, 524 (1912).

Experimental.

o-Uramino-benzoic Acid (**o-Ureido-benzoic Acid**), $H_2N.CO.NH.C_6H_4.COOH$, was prepared first by Griess[1] by the interaction of anthranilic acid and potassium isocyanate in presence of hydrochloric acid, but he gave no details of his process or description of his product, other than to note that it crystallized in small, white needles. Gabriel and Colman[2] later prepared it in much the same way and obtained a fine, crystalline powder.

Twenty-seven g. of anthranilic acid was treated with 20 cc. (calculated, 16 cc.) of conc. hydrochloric acid, the mixture dissolved in a liter of hot water, filtered and the filtrate cooled. A solution of 20 g. (calculated, 16 g.) of potassium isocyanate in 50 cc. water was added slowly with mechanical stirring. When about half of the cyanate solution had been run in, the mixture suddenly set to a pasty mass of crystals. After all the cyanate had been added, the mixture was left overnight, the precipitate filtered out, washed with water and dried on a porous tile. Microscopic, colorless needles, decomposing at 162–4° (corr.), were thus obtained. Yield, 27.3 g. or 72.7% of the theoretical amount. The compound was purified by dissolving it in absolute methyl or ethyl alcohol at room temperature, stirring with animal charcoal, filtering, and concentrating the filtrate *in vacuo* at 10–20°. The purified acid separated in tufts of fine, colorless, silky needles, decomposing at 171–2° (corr.) with formation of benzoylene urea. It is so rapidly changed into benzoylene urea by the action of heat, of alkali or of mineral acid, that it cannot be purified satisfactorily either by crystallization from hot solvents or by solution in alkali and reprecipitation by mineral acid.

Subs., 0.1609, 0.2571: 21.60 cc. N at 21° and 763.7 mm., 33.85 cc. N at 18° and 766.7 mm.

Calc. for $C_8H_8O_3N_2$: N, 15.52. Found: 15.34, 15.27.

It is practically insoluble in ligroin; very slightly soluble in water, carbon tetrachloride, carbon disulfide or cold toluene; somewhat more soluble in chloroform, benzene or hot toluene; moderately soluble in ether; and dissolves readily in methyl or ethyl alcohols, acetone or ethyl acetate. Hot water decomposes it.

It is very easily condensed to benzoylene urea by a variety of reagents. Heated in an oil bath to 190–200°, it yields 30% of the theoretical amount, while conc. aqueous sodium hydroxide gives nearly a quantitative yield.

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[1] *J. prakt. Chem.*, [2] **5**, 371 (1872).

[2] *Ber.*, **38**, 3561 (1905).

Gabriel and Colman[1] have shown that heating with 20% aqueous hydrochloric acid also causes this condensation.

Methyl Ester.—The condensation of methyl anthranilate with potassium isocyanate could not be carried out in hydrochloric acid solution, for the reason that the concentration of acid necessary to get the anthranilate into solution decomposed the cyanate; and, as the acid concentration diminished, the unchanged methyl anthranilate separated as an oil. Acetic acid, therefore, was substituted for hydrochloric acid, and the reaction then ensued smoothly and without difficulty. From 20 g. of methyl anthranilate, 600 cc. of 50% acetic acid and 12 g. (calc., 10.9 g.) of potassium isocyanate, 26 g. of methyl uramino benzoate was obtained, which is the theoretical yield. Purified by crystallization from methyl alcohol, it formed glistening, white needles, melting with decomposition at 177–7.5° (corr.).

Subs , 0.1816 23 00 cc N at 20° and 761 2 mm

Calc for $C_9H_{10}O_3N_2$· N, 14 42. Found: 14 44

Its solubilities are much the same as those of the free acid. When heated above its melting point, or boiled with water, it gives off odors resembling those of methyl anthranilate and methyl salicylate, but the chief product is always benzoylene urea. The latter is also formed when the ester is dissolved in 30% aqueous sodium hydroxide solution or in conc. sulfuric acid, or when it is treated for a few hours with a saturated solution of ammonia in water, methyl or ethyl alcohol, ether or benzene. In no case was there any evidence of amide formation, as the result of the action of ammonia upon the ester.

Benzoylene Urea (2,4-Diketo-tetrahydro-quinazoline), $\overline{NHCONHC_6H_4CO}$.—Of the various methods which have been used for the preparation of benzoylene urea, the most promising seemed to be the fusion of anthranilic acid with urea[2] and the condensation of *o*-uraminobenzoic acid.

The first experiments, therefore, were concerned with the urea method. It is believed that the benzoylene urea formed in this process owes its origin to the following changes:

$$H_2NC_6H_4COOH + H_2NCONH_2 \longrightarrow H_2NCONHC_6H_4COONH_4 \longrightarrow$$
$$H\overline{NCONHC_6H_4CO} + H_2O + NH_3,$$

inasmuch as the *meta*- and *para*-aminobenzoic acids give the corresponding uramino-benzoic acids when fused with urea,[3] ammonia is evolved during the fusion quite freely, and we have shown that both uramino-benzoic acid and its ammonium salt yield benzoylene urea when heated. Further, Paal[1] has proven that *o*-phenyluramino-benzoic acid gives 3-phenylbenzoylene urea, and Pawleski[2] has produced the same substance by fusing anthranilic acid with monophenyl urea. In fact, Weiland[3] states that uramino acids are formed by heating together amino acids and urea, in neutral aqueous solution, even at 42–5°.

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[1] *Loc. cit.*

[2] Griess, *Ber.*, 2, 416 (1869); *J. prakt. Chem.*, [2] 5, 371 (1872). See also Abt., *J. prakt. Chem.*, [2] 39, 143 (1889) and Pawlewski, *Ber.*, 38, 130 (1905).

[3] Griess, *J. prakt. Chem.*, [2] 5, 369 (1872).

In testing the stability of anthranilic acid to heat, it was ascertained that it begins to sublime and to give off carbon dioxide at its melting point (145°), the evolution of gas being quite rapid at 160–5°.

If the temperature is carried too high during the fusion of anthranilic acid and urea, some of the benzoylene urea already formed is decomposed into anthranilic nitrile and carbon dioxide.[4]

In spite of numerous trials and a careful study of the various factors involved, the yields could not be raised above 46% of the theoretical amount. Further, with increasingly large amounts the yields grew steadily poorer, presumably because of the difficulty in heating the larger melts uniformly. As products of the reaction, in addition to benzoylene urea, there were identified, water, ammonia, carbon dioxide and ammonium carbamate, and evidence was obtained also of the presence of anthranilic nitrile and of biuret. As Werner[5] has shown, when urea is heated it suffers decomposition into ammonia and isocyanic acid, at temperatures just above its melting point (132°), some of the latter then polymerizing to cyanuric acid and some combining with unchanged urea to form biuret. At higher temperatures (190–200°), some ammelide is produced, but we did not discover any of this compound in our melts.

By the action of strong aqueous sodium hydroxide upon *o*-uraminobenzoic acid, benzoylene urea can be prepared rapidly and in any desired amount, as already described in our previous article.

From water or dil. acetic acid, it separates in colorless needles, and from glacial acetic in small plates. By careful and repeated crystallization, a melting point of 353–4° (corr.) was obtained, and this could not be raised by further crystallization. It sublimes unchanged at high temperature. Its solubility at 23° is 0.000741 mole (0.129 g.) per liter of water. It is difficultly soluble in ethyl alcohol, and but slightly soluble in amyl alcohol or in carbon tetrachloride. By direct nitration, it gives 6-nitro- and 6,8-dinitro-benzoylene urea. Fused with oxalic acid, it gives no carbazole blue reaction.

[1] *Ber.*, **27**, 978 (1894)

[2] *Ibid.*, **38**, 130 (1905) See also Kunckell, *Ibid*, **38**, 1213 (1905) and **43**, 1237 (1910).

[3] *Chem. Zentr.*, **1912**, I, 1230.

[4] Compare Abt, *J. prakt. Chem.*, [2] **39**, 143 (1889) and Haslinger, *Ber.*, **41**, 1451 (1908).

[5] *J. Chem. Soc.*, **103**, 1010, 2275 (1913)

Sodium Salt.—Purified by repeated crystallization from dil. aqueous sodium hydroxide, this salt was obtained in long, white needles, containing water of crystallization which was lost at room temperature *in vacuo* over sulfuric acid.

Subs., 1.0032; Na_2SO_4, 0.3824.
Calc. for $C_8H_5O_2N_2Na$: Na, 12.50. Found: 12.34.

The solubility of this salt at 23° was determined by taking a measured volume saturated at that temperature, heating to boiling, acidifying with hydrochloric acid, cooling, filtering out the precipitated benzoylene urea, and drying it to constant weight in a Gooch crucible at 120°. This gives the difference in solubility between the benzoylene urea itself and its sodium salt.

100 cc. of solution saturated at 23° gave 0.7024 g. benzoylene urea, indicating a solubility of 0.0433 mole per liter, or 0.7967 g. $C_8H_5O_2N_2Na$ per 100 cc., assuming the solubility of the free benzoylene urea to be practically zero

6-Nitro-benzoylene Urea, $\overline{NHCOC_6H_3(NO_2)NHCO}$, was prepared by the direct nitration of benzoylene urea, and also by the action of aqueous ammonia upon methyl-dinitro-uramino-benzoate. It could not be obtained by the fusion of 5-nitro-anthranilic acid with urea, nor by the action of ammonia upon the free dinitro-uramino-benzoic acid. This is in harmony with the experience of Lederer[1] who heated an intimate mixture of urea and 5-nitro-2-anilino-benzoic acid at 205°, without accomplishing any quinazoline condensation, the nitro-phenylanthranilic acid being recovered unchanged.

Twenty g. of benzoylene urea was dissolved in 200 cc. of conc. sulfuric acid, and the calculated amount (5.4 cc.) of fuming nitric acid (sp. gr. 1.5) was added slowly. The temperature rose to about 50°. The mixture was then heated for an hour on the water bath, cooled, poured upon ice, the precipitate filtered out, washed, and crystallized from 50% acetic acid (1 liter), in presence of animal charcoal. It formed brownish yellow prisms, decomposing at 326–30° (corr.). Yield 14.5 g., or 56.5% of the theoretical amount. Much was left in the mother liquor.

The crude material was purified by dissolving it in excess of hot dilute aqueous sodium hydroxide, crystallizing the sodium salt thrice from water, reconverting it to the free nitro compound by acidifying the hot solution with acetic acid, and recrystallizing from 50% acetic acid to constant decomposition point. There resulted pale, greenish yellow prisms, decomposing at 330–1° (corr.); moderately soluble in hot methyl alcohol or in boiling glacial acetic acid; slightly soluble in hot water, ethyl alcohol, ethyl acetate, acetone, ether or toluene; and practically insoluble in chloroform, carbon tetrachloride, carbon disulfide, ligroin or benzene.

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[1] Rostock, *Inaug. Diss.*, 1906, p. 60.

The same compound was obtained by the following process: One g. of methyl-dinitro-uramino-benzoate was suspended in 20 cc. of water in a pressure bottle and the liquid saturated with ammonia at 0°. It was then heated at 100° for 4 hours, cooled in a freezing mixture, the bottle opened, excess of ammonia driven out by heating on the steam bath, 60 cc. of water added, the solution acidified hot with acetic acid, and allowed to cool. The bright yellow prisms which separated were filtered out, washed with water, and dried at 120°. Yield, 0.75 g., or 100% of the theoretical amount. These crystals were powdered, extracted thrice with boiling alcohol, and recrystallized from glacial acetic acid. The product was identical with the 6-nitro-benzoylene urea obtained by direct nitration as described above.

Subs., 0.1884: 34 62 cc. N at 21.3° and 751.2 mm.
Calc. for $C_8H_5O_4N_3$: N, 20.29. Found: 20.54.

Fifty years ago, Griess[1] reported that when benzoylene urea was treated with nitric acid he obtained a mononitro derivative crystallizing in honey-yellow prisms. He gave no further description of his process or product, but there can be little doubt that it was the 6-nitro derivative.[2]

Sodium Salt.—Long, light greenish yellow needles, containing no water of crystallization. Its aqueous solutions are yellow and it is reprecipitated from such solution by carbon dioxide. Heated dry, it chars without explosion.

0.240 g. of the salt was dissolved in 100 cc. of boiling water. On cooling, a small amount precipitated, leaving a saturated solution of strength slightly less than 0.01 molar. Five drops of this solution were added to 10 cc. of phosphate and borate solutions (Sörensen standard). The solution with index 7 (Sörensen scale) was colorless, and a greenish yellow color developed very slowly from 7.5 until index 11 was reached, and then rapidly up to that with index 13. The development of color was too slow for this salt to be of any use as an indicator.

6,8-Dinitro-benzoylene-urea, $\overline{NHCOC_6H_2(NO_2)_2NHCO}$, was obtained by the direct nitration of benzoylene urea and of its 6-nitro derivative. Its production from benzoylene urea itself is set forth in our earlier paper.

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[1] *Ber.*, 2, 416 (1869).

[2] Griess did state that reduction of this nitro derivative by ammonium sulfide, or by tin and hydrochloric acid, yielded an amino derivative crystallizing in pale yellow needles, difficultly soluble in all neutral solvents, and which combined with acids to give salts which in most cases crystallized well and were very difficultly soluble.

In 1905, Kunckell (*Ber.*, 38, 1213 (1905)) announced that he had nitrated benzoylene urea, reduced the nitro to the amino derivative, and prepared various compounds from the latter, on all of which he expected to report later, since Mr. Lederer, one of his Ph.D. candidates, was engaged upon this investigation. No subsequent publication on this research by Kunckell has been located, and the dissertation of Karl Lederer, *Ueber einige Derivate des Ketotetrahydrochinazolins*, Rostock, 1906, fails to record any work upon the nitration of benzoylene urea or the reduction of any nitro derivatives thereof.

The preparation from the mononitro derivative was carried out as follows: One g. of 6-nitro-benzoylene urea was dissolved in 10 cc. of conc. sulfuric acid, and 6 cc. (calc., 4 cc.) of conc. nitric acid added. The yellow solution turned red upon the addition of the nitric acid, but soon changed to yellow again. After an hour's heating on the steam bath, it was cooled, poured into 100 cc of cold water, and the precipitated dinitro derivative purified in the manner described in our other paper. The following additional observations were made on this compound:

Mixed with soda lime, it gives a brick-red color which changes to orange on exposure to the moisture of the atmosphere. This mixture explodes when heated, with evolution of ammonia, and the residue chars. When 2 g. of the compound was dissolved in a solution of 10 g. sodium hydroxide in 30 cc of water, there resulted a bright red solution and an orange precipitate. On short boiling of this mixture, both solution and precipitate turned black and considerable ammonia was given off. After 12 hours' boiling, the mixture was acidified with hydrochloric acid, but only a slimy, black precipitate was obtained, from which no pure compounds could be recovered.

The anhydrous monosodium salt is orange, and when heated turns red and finally explodes. Its other properties are given in our former paper.

The potassium and ammonium salts, prepared in similar manner, resemble the sodium salt in appearance and general behavior, except that the ammonium salt decomposes without explosion. The solubilities of these salts were determined at 20° by the method used for the sodium salt.

(1) 50 cc solution of the potassium salt saturated at 20° gave 0.1791 g of dinitrobenzoylene urea, indicating a solubility of 0.0142 mole per liter

(2) 50 cc solution of the ammonium salt saturated at 20° gave 0.2656 g of dinitrobenzoylene urea, indicating a solubility of 0.0211 mole per liter.

6,8-Diamino-benzoylene Urea.—80 g. (calc. 45 g.) of stannous chloride was dissolved in 300 cc. of conc. hydrochloric acid, the solution heated to boiling, 10 g. of dinitro benzoylene urea added slowly, and the solution boiled for 4 hours. On cooling, the hydrochloride of the diamine separated in bunches of pink prisms, which were filtered out, washed with water, dried at 120°, boiled 15 minutes with 50 cc. of conc. hydrochloric acid, the solution diluted with an equal volume of water, boiled a few minutes longer, cooled, the precipitate filtered out, heated with 300 cc. of freshly boiled water and made alkaline with ammonia. The result was a yellow precipitate and a yellow solution with greenish fluorescence. Yield of diamine, 6 g., or 78.9% of the theoretical amount.

Crystallized from freshly boiled water containing some ammonia, it separates in long, dull, yellow needles, which darken at about 200° and decompose at 335° (corr.). Treatment with freshly boiled water made slightly acid with acetic acid did not alter the appearance or the decomposition point.

Subs., 0.1292: 34.38 cc. N at 24.5° and 747.2 mm.
Calc. for $C_8H_8O_2N_4$: 29.15. Found: 29.11.

The compound is slightly soluble in boiling water, but practically insoluble in cold water or in the other ordinary solvents. It gives a very difficultly soluble hydrochloride. In hot dil. sodium or ammonium hydroxide solutions it dissolves somewhat, apparently with the formation of easily hydrolyzable salts. Its alkaline solution soon turns red, due to oxidation, and a flocculent violet precipitate separates, which turns black when dried and is insoluble in all common solvents. This oxidation ensues still more rapidly in neutral or faintly acid solutions. In dil. acids, it gives a purple solution in which the purple precipitate forms more slowly. Distillation with soda lime completely breaks down the compound.

2,4-Dichloro-quinazoline, $\overline{\mathrm{N:CCl.C_6H_4.N:CCl}}$, was prepared from benzoylene urea, phosphorus oxy- and pentachlorides, by the method of Gabriel and Colman[1] and was purified by distilling off the phosphorus halides under diminished pressure, as recommended by Abt.[2] Yield of crude product, 82% of the theoretical amount. This was fully pure enough for most purposes and was used in subsequent syntheses.

A sample very carefully purified by recrystallization from benzene and distillation under reduced pressure, formed white, lustrous blades, melting point 119.5° (corr.). Abt gives the melting point as 115°. Crystallization from benzene alone is not very satisfactory, on account of the small temperature coefficient of solubility.

2,4-Dimethoxy-quinazoline was obtained from the dichloro derivative by following the directions of Bogert and May.[3] Yield, 26.5% of the theoretical amount. By very careful purification, involving distillation with steam and recrystallization, long, white, silky needles were secured, m. p. 74°, which melting point could not be raised by further crystallization from dil. alcohol. Abt[4] gives the melting point as 66°; Bogert and May, as 67°. It was further proven that this high melting point was not due to any admixture of 1,3-dimethyl-benzoylene urea, as the latter is not volatile with steam, and the addition of some of it to the dimethoxy derivative lowered the melting point to 69.5–71.5°.

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[1] *Ber.*, 38, 3559 (1905).

[2] *J. prakt. Chem.*, [2] 39, 140 (1889).

[3] THIS JOURNAL, 31, 512 (1909).

[4] *Loc. cit.*

1,3-Dimethyl-benzoylene urea, $CH_3\overline{NCOC_6H_4N(CH_3)CO}$, was prepared first by Abt[1] by the direct methylation of benzoylene urea, or of its 1- or 3-monomethyl derivative, with methyl iodide. Later, it was produced in much the same way by Bogert and May.[1]

On repeating the process, the crude product was crystallized from 50% alcohol, giving slender, white needles, melting point 153–6° (corr.). These crystals were boiled for 15 minutes with 60 cc. of conc. hydrochloric acid, to hydrolyze any methoxy derivatives, the solution made slightly alkaline with sodium hydroxide, diluted with water, the crystals filtered out, washed and dried. Slender, white needles resulted, m. p. 167–8° (corr.). Abt gives the melting point of this compound as 151°, Bogert and May, as 163–5°. The melting point of our product could not be raised further by recrystallization, nor by a second treatment with hydrochloric acid followed by recrystallization. Yield of crude product, 94% of the theoretical amount.

The alkaline filtrate from the first hydrochloric acid treatment was acidified with the same acid, the precipitate filtered out, washed, dried and crystallized from dil. alcohol. Fine, white needles, m. p. 237–8° (corr.), were thus obtained, which contained no halogen. Abt gives the melting point of 3-methyl-benzoylene urea as 234°, as does also Soderbaum.[2] The second treatment of dimethyl-benzoylene urea with hydrochloric acid yielded no monomethyl derivative. The amount of monomethyl recovered from the crude dimethyl derivative was always considerable. Its origin is evidently to be ascribed to the incomplete methylation of the benzoylene urea, inasmuch as pure 1,3-dimethyl-benzoylene urea is unchanged by boiling hydrochloric acid, and because we obtained the same compound from benzoylene urea and one mole of methyl iodide.

1,3-Dimethyl-benzoylene urea is not appreciably volatile with steam nor is it changed by 4 hours' boiling with fuming nitric acid and conc. sulfuric acid.

3-Methyl-benzoylene Urea.—Abt reported that with one mole of alcoholic sodium hydroxide, he obtained a monosodium salt, carrying alcohol of crystallization, which yielded 1-methyl-benzoylene urea (melting point 147–8°) on treatment with methyl iodide. Our results do not tally with this, for we found that limited methylation of benzoylene urea gave the 3-methyl and not the 1-methyl derivative.

Eight g. of benzoylene urea and the calculated amount (2 g.) of sodium hydroxide were dissolved in 250 cc. of 50% methyl alcohol by warming. The solution was cooled to room temperature, causing the monosodium salt of benzoylene urea to separate; 8 g. (calc. 7 g.) of methyl iodide was added, the solution boiled under a reflux condenser until all the methyl iodide had disappeared (3 hours), filtered hot, and the filtrate cooled. The crystals which separated were filtered out, washed, dissolved in 150 cc. of 0.7 molar sodium hydroxide solution, the solution filtered, the filtrate acidified with hydrochloric acid, the precipitated crystals removed, washed, and dried at 110°. Yield, 7.5 g., or 80% of the theoretical amount. This crude product was recrystallized from alcohol, giving slender, white needles, melting point, 230–3° (corr.). Mixed with 3-methyl-benzoylene urea from the preparation of the 1,3-dimethyl derivative, a melting point of 230–6° (corr.) was obtained.

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[1] *Loc. cit.*

[2] *Ber.*, 23, 2183 (1890).

Since the purpose of this synthesis was to identify the monomethyl derivative formed in the preparation of the dimethyl, it was not further purified. In the synthesis it is advisable to use some excess of methyl iodide, since it is much easier to free the 3-methyl derivative from dimethyl than from benzoylene urea itself.

From the first filtrate, acidified with hydrochloric acid, a small amount (0.4 g.) of 1,3-dimethyl-benzoylene urea was recovered.

3-Methyl-benzoylene urea was unchanged by 4 hours' boiling with fuming nitric and conc. sulfuric acids.

5-Nitro-2-nitrouramino-benzoic Acid (Dinitro *o*-Uramino-benzoic Acid), $(2)O_2NNHCONHC_6H_3(NO_2)(5)COOH(1)$.—In 1878, Griess[1] reported that the action of nitric acid upon *o*-uramino-benzoic acid yielded but one dinitro derivative, and that this product resembled in its general behavior the isomeric dinitro derivatives of the *meta* and *para* series. He gave no analytical figures or further characterization of the new dinitro acid, except the statement that when boiled with water it yielded 5-nitro-anthranilic acid, nitrous oxide and carbon dioxide. This work we have repeated and confirmed.

Sixty cc. of fuming nitric acid (sp. gr. 1.5), free from lower oxides of nitrogen was cooled to —5° to —10° and 7.5 g. of *o*-uramino-benzoic acid added slowly. At the end of an hour, the mixture had changed to a pasty mass, which was allowed to stand for 3 hours at a temperature below 0°, then poured upon 500 g. of ice and filtered immediately. A yellowish solid resulted, which softened at 170° and largely distilled to a bright, yellow liquid, the residue decomposing at about 230°. Yield, 8 g., or 76.3% of the theoretical amount.

Considerable difficulty was experienced in endeavoring to free the product from the nitro-anthranilic acid into which water slowly decomposes it. After digestion with boneblack in anhydrous acetone solution and repeated crystallization from the same solvent, pale greenish yellow plates were obtained, decomposing at 256–8° (corr.). One fraction charred without melting at 286–95° (corr.), the others gave a constant decomposition point after several recrystallizations, and a mixture of the two decomposed partially at 256–8° (corr.), the remainder charring at 286–95° (corr.). Both forms gave 5-nitro-anthranilic acid when boiled with water.

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[1] *Ber.*, 11, 1730 (1878).

Analytical figures were not obtained, for the reason that the small amount of purified material available was lost through repeated explosions in the combustion tubes.

The substance is more or less readily soluble in methyl or ethyl alcohol, acetone, ethyl acetate or glacial acetic acid; but is practically insoluble in ether, benzene, toluene, ligroin, chloroform, carbon tetrachloride or carbon disulfide. It crystallizes from glacial acetic acid in flat prisms, decomposing at 255–60° (corr.). In boiling water, it dissolves, but yellow needles of 5-nitro-anthranilic acid soon separate; cold water acts similarly but more slowly. The action of saturated aqueous ammonia at 100° gave a mixture of products which were not separated or identified further than to prove that no nitro- or dinitro-benzoylene urea was present.

Methyl Ester.—Eighty cc. of fuming nitric acid (sp. gr. 1.5), free from lower oxides, was cooled to —5° to —10°, and 10 g. of methyl-*o*-uramino-benzoate added slowly. The mixture was allowed to stand for 4 hours, then poured upon 400 g. of ice and filtered immediately. The precipitate when spread on a porous plate appeared as a pasty, salmon-colored mass, turning to buff when fully dried. Crystallized from alcohol, in presence of animal charcoal, pale greenish yellow rhombic plates were obtained, decomposing at 184–5° (corr.) to yellow crystals which melted at 217–33° (corr.), neither of which points was changed by recrystallization of the ester from absolute or diluted alcohol. Yield, 7.5 g., or 52% of the theoretical amount.

Subs., 0.1631: 28.10 cc. N at 18.5° and 757.2 mm.
Calc. for $C_9H_8O_7N_4$: N, 19.72. Found: 19.68.

The compound is practically insoluble in chloroform, carbon tetrachloride, carbon disulfide, acetone or cold water. It is slightly soluble in ligroin or benzene; and more or less easily soluble in methyl or ethyl alcohol, glacial acetic acid, ethyl acetate or toluene. Boiled with water, it gives methyl-5-nitro-anthranilate.

The dry substance when heated puffed suddenly at about 180–5° (corr.) with formation of yellow vapors. The residue gave 36% of the theoretical yield of methyl-5-nitro-anthranilate, together with small amounts of other products which were not identified. No attempt was made to identify the impure crystalline yellow product (m. p. 217–33°) resulting from the action of heat upon the ester, other than to establish the fact that it was not a nitro-benzoylene urea. Treatment of the ester with conc. aqueous sodium hydroxide or sulfuric acid also gave mixtures of various undetermined products, but among which there was no nitro-

or dinitro-benzoylene urea. By the action of conc. aqueous ammonia upon the ester, however, 6-nitro-benzoylene urea was obtained.

5-Nitro-2-acetamino-benzoic Acid (5-Nitro-acetanthranilic Acid), (2)$CH_3CONHC_6H_3(NO_2)$(5)COOH(1).—5-Nitro-2-acetamino toluene (5-nitro-2-acetotoluide) was prepared from C. P. 5-nitro-2-toluidine (m. p. 129.5–32°, corr.) by direct acetylation with acetic anhydride in glacial acetic solution. Yield, practically the theoretical amount. Pale yellowish, silky needles (from alcohol), melting point 197.5–8° (uncorr.), or 204.–4.5° (corr.), as reported by Bogert and Cook.[1]

From this acetamino derivative, 5-nitro-2-acetanthranilic acid was obtained by oxidation with potassium permanganate, following the process of Bogert and Cook, in light yellow prisms (from water), melting point 218° (corr.). Yield, 65.5% of the theoretical amount. Some nitro-anthranilic acid was recovered from the filtrate.

Barium Salt.—Bright yellow tufts of fine hairs, or flat prisms; slightly soluble in cold water, easily in hot.

Calcium Salt.—Similar to the barium salt, except that it crystallizes in needles.

Ferric Salt.—Dull, chocolate, gelatinous precipitate, only slightly soluble in hot water, from which it separates in amorphous condition.

Cupric Salt.—Light green, gelatinous precipitate, crystallizing from water in fine, green hairs. Soluble in ammonium hydroxide solutions.

Lead Salt.—Bright yellow precipitate, crystallizing from water in balls of hair-like needles.

Silver Salt.—Curdy, light yellow precipitate, resembling silver iodide, and crystallizing from water in sheafs of hair-like needles.

Many of the statements in the literature concerning this acid are, to say the least, confusing.

Rupe[2] by direct nitration of acetanthranilic acid with mixed acids at about 40°, claimed to have obtained the 5-nitro derivative, and gave a melting point of 152° for his acid. We have repeated Rupe's process and by frequent crystallization of the product from water have obtained a substance melting at 174–7° (corr.), which was evidently still impure, its impurities being probably nitro-anthranilic acid formed by de-acetylation[3] and *p*-nitraniline formed by loss of carbon dioxide from the latter.

Ullmann and Uzbachian[4] make the astonishing announcement that they prepared 5-nitro-acetanthranilic acid by oxidation of 4-nitro-acetotoluide of melting point 151°. This may have been due to an error in copying, with the melting point filled in from Beilstein and not from the laboratory note book, as the acid obtained was evidently the 5-nitro derivative.

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[1] This Journal, 28, 1451 (1906).

[2] *Ber.*, 30, 1097 (1897).

[3] Compare Seidel and Bittner. *Monatsh.*, 23, 435 (1902).

[4] *Ber.*, 36, 1797 (1903).

Baly, Tuck and Marsden[1] prepared the acid both by oxidation of the nitro-acetotoluide with potassium permanganate and by direct nitration of acetanthranilic acid, claiming a yield by the latter method of 85%. They failed to record the melting point of their products, however. Numerous repetitions of this direct nitration method, have failed to yield us pure products, the results being much the same as from the Rupe method. By nitrating at lower temperatures, however, a fairly good product was secured.

Ten g. of acetanthranilic acid was added slowly to 20 cc. of fuming nitric acid (sp. gr., 1.5), keeping the temperature below 5°. The mixture was maintained at that temperature for 4 hours, then for 2 hours at laboratory temperature, when a red color developed. It was poured upon ice and the light yellow precipitate recrystallized from alcohol in presence of animal charcoal. Yield, 5 g., or 39% of the theoretical amount; melting point, 206–10° (corr.). Further recrystallization from alcohol raised the melting point to 214–5° (corr.). This product was hydrolyzed to nitro-anthranilic acid without further purification.

5-Nitro-2-amino-benzoic acid (5-nitro-anthranilic acid), was prepared according to the process of Rupe[2] by boiling the foregoing acetyl derivative with conc. hydrochloric acid and recrystallizing the product from the dil. acid. Long, bright yellow needles were thus secured, which blackened at 240–50° (corr.), and melted with decomposition at 275–6° (corr.). Yield, 98% of the theoretical amount.

The pure acid separates from 95% alcohol in pale yellow, satiny blades; from water, or dilute alcohol, in fine, golden yellow needles. Recrystallized to constant decomposition point, it decomposes at 278° (corr.), with blackening and some sublimation above 240°. As the decomposition point varies considerably depending upon the rapidity of the heating, it is not surprizing that the melting point (really decomposition point) recorded in the literature shows a confusing range, being variously stated from 261° to 280°.

The solubilities of the acid were determined roughly at laboratory temperature (about 18°) by taking a known volume of saturated solution, evaporating to dryness and weighing the residue. The results expressed in g. per liter were as follows: water, 1.0; glacial acetic acid, 3.0; mixture of glacial acetic acid and ethyl acetate (50: 50), 4.0; ether, 7.0; ethyl acetate, 7.5; alcohol, 14.0; boiling glacial acetic acid, 15.0–20.0.

Salts.—The sodium, potassium and ammonium salts are moderately soluble in cold water, easily soluble in hot. All form fine, brownish orange needles, those of the sodium salt being rather darker than the other two.

Methyl Ester.—This was formed by esterification of the acid with either methyl alcohol and hydrochloric acid, or with methyl sulfate. Yield by the former method, 61% of the theoretical amount; by the latter, 46.5%.

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[1] *J. Chem. Soc.*, 97, 1502 (1910).

[2] *Loc. cit.*

Recrystallized from slightly diluted alcohol until the melting point remained constant, it formed pale yellow needles of greenish tinge, melting point 168° (corr.), difficultly soluble in cold water, more or less readily soluble in the other ordinary solvents. It is slowly volatile with steam with partial decomposition, and can be sublimed unchanged.

Subs., 0.1457: 18.32 cc. N at 19.5° and 765.0 mm.
Calc. for $C_8H_8O_4N_2$: N, 14.29. Found: 14.43.

All efforts to convert this ester into the amide by the action of ammonia proved fruitless, the ammonium salt of the acid being the only product. This coincides with the experience of Thieme[1] in the case of the ethyl ester.

6-Nitro-4-quinazolone, $\overline{\mathrm{NHCOC_6H_3(NO_2)N{:}C}}\mathrm{H}$.—A mixture of 10 g. of 5-nitro-anthranilic acid and 10 g. of formamide (calc. 2 g.) was fused at 150–70° for 6 hours, the melt cooled, extracted with 40 cc. of cold water, and the residue crystallized from 50% acetic acid. Light brown prisms resulted, melting point 283–5° (corr.). Yield, 3.5 g., or 33.4% of the theoretical amount. Dissolved in alkali and reprecipitated with acetic acid, pale brownish crystals were obtained, m. p. 286–7° (corr.).

Bogert and Geiger[2] nitrated 4-quinazolone and obtained a nitro derivative, m. p. 286.5–7.5° (corr.), which they believed to be the 6-nitro-4-quinazolone. The compound prepared from 5-nitro-anthranilic acid, as described above, proved to be identical in all respects with the product of Bogert and Geiger, and the melting point of a mixture of the two was 285.5–6.5° (corr.). This supplies the synthetic proof that the product of direct nitration of 4-quinazolone is really the 6-nitro derivative.

Experiments on the availability of this compound as an indicator showed that its range of color change was from index 7 to 9.3, and the change from colorless to greenish yellow. To get a satisfactory color, it was found necessary to use 10 drops of a 0.05 molar solution. This is too concentrated for good results, and the free nitro-quinazolone was precipitated in acid solutions.

6-Nitro-2-methyl-4-quinazolone was also tested for use as an indicator. Its range of color change proved to be from index 7.2 to 9.5. Otherwise, it behaved exactly like the 6-nitro-4-quinazolone.

Summary.

1. A further study has been made of the preparation and properties of benzoylene urea, and of the following derivatives: 6-nitro, 6,8-dinitro, 6,8-diamino, 3-monomethyl and 1,3-dimethyl

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[1] *J. prakt. Chem.*, [2] 43, 470 (1891).

[2] THIS JOURNAL, 34, 524 (1912).

2. In the methylation of benzoylene urea, results have been obtained differing from those of Abt.

3. Dichloro- and dimethoxy-quinazoline have been prepared in purer form than hitherto.

4. Our knowledge of *o*-uramino benzoic acid and of its dinitro derivative has been extended.

5. 5-Nitro-anthranilic acid and its acetyl derivative have been studied and some of the existing confusion in the literature cleared up.

6. The structure of 6-nitro-4-quinazolone has been proven by its synthesis from 5-nitro-anthranilic acid.

7. The serviceability of certain quinazolines as indicators has been tested.

8. The following new compounds have been prepared: methyl-*o*-uramino benzoate, the sodium salt of 6-nitro-benzoylene urea, the potassium and ammonium salts of 6,8-dinitro-benzoylene urea, methyl-dinitro-*o*-uramino benzoate, various salts of 5-nitro-acetanthranilic acid and of 5-nitro-anthranilic acid, and the methyl ester of the latter.

NEW YORK, N. Y.

[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE STATE UNIVERSITY OF IOWA.]

MOLECULAR REARRANGEMENT IN THE ACYLATION OF CERTAIN AMINOPHENOLS.

BY L. CHAS. RAIFORD.

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During the course of a research now in progress in this laboratory, the purpose of which is the study of the steric relations involved in the acylation of aminophenols, it became necessary in the identification of one of the products isolated to prepare a diacylated derivative of an *o*-aminophenol in which the acyl radicals bound to oxygen and to nitrogen, respectively, were different. In the case under consideration the two radicals were acetyl and benzoyl. It may be stated at the outset that further examination of the product showed that the heavier of these radicals, benzoyl in this case, was always found attached to nitrogen, regardless of the order in which they were introduced, which indicates that a rearrangement must have occurred in one case.

As will appear below, the rearrangement in this case involved the migration of acetyl from nitrogen to oxygen, and possibly the shift of benzoyl in the opposite direction, though the mechanism of the reaction has not yet been satisfactorily determined. The migration of acyl from oxygen to nitrogen has previously been observed in several different cases, following the work of Böttcher[1] on 2-benzoyl-aminophenol.[2] The replacement of a lighter acyl radical (acetyl) by a heavier one (*m*-nitrobenzoyl) was recorded by Torrey and Kipper[1] and the migration of acyl from nitrogen to oxygen has been observed by Willstätter and Veraguth[2] and by Auwers;[3] but, so far as the writer is aware, the exact behavior described in the present research has not hitherto been reported. Ransom,[4] it is true, has prepared diacylated *o*-aminophenols in which the acyl groups are different, and Ransom and Nelson[5] as a result of further study of the reactions involved, state "that when two carboxyl radicals (COOR and $COOR_1$) are introduced into the molecule of *o*-aminophenol the lighter one becomes attached to nitrogen, the position not being influenced by the order in which the groups are introduced; and that to accomplish this, a molecular rearrangement occurs in one case. This is also true when both of the radicals are carbonyls (COR and COR_1)." In the light of these statements the results obtained in the research described below were unexpected, and this made it a matter of much interest to determine whether the present observation represented merely an isolated case or was an example of a more general reaction.

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[1] *Ber.*, 16, 629 (1883).

[2] For a bibliography of the subject see Weyl, "Die Methoden der Organischen Chemie," II, p. 1281; Leipzig, 1911 (Thieme).

The base employed in the first experiments was 2-amino-4-methyl-6-bromophenol.[6] When this was warmed with anhydrous sodium acetate and the necessary amount of acetic anhydride, in the usual way, it was converted into a diacetyl derivative. Treatment of the latter with a cold dilute solution of sodium hydroxide caused saponification to take place rapidly at the *o*-connection, giving 2-acetylamino-4-methyl-6-bromophenol. When this phenol was subjected to the Schotten-Baumann reaction with benzoyl chloride, the reaction proceeded smoothly and rapidly to give an acetyl-benzoyl derivative. Saponification of the latter product with alkali took place somewhat more slowly than was the case with the diacetyl derivative, and the phenolic substance that resulted was not the 2-acetylamino-4-methyl-6-bromophenol which was used in preparing the acetyl-benzoyl derivative, and which one might expect to obtain if saponification again took place at the *o*-connection and no rearrangement had occurred, but 2-benzoylamino-4-methyl-6-bromophenol. The identity of the last named product was established by synthesizing it in a wholly different way, *viz.*, by treatment of an ethereal solution of the free aminophenol with benzoyl chloride as described by Ransom,[7] and by showing that the benzoyl derivative thus obtained could readily be converted, by acetylation in the usual way, into the acetyl-benzoyl derivative whose structure was in question. From these reactions it appears that the rearrangement occurred during the introduction of the benzoyl radical into 2-acetylamino-4-methyl-6-bromophenol, and not during the saponification of the resulting acetyl-benzoyl compound. Similar results were obtained when these experiments were repeated, using 2-amino-4,6-dibromophenol as the starting base (see experimental part). The reactions involved with the first of these bases may be briefly summarized as follows:

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[1] This Journal, 30, 859 (1908).

[2] *Ber.*, 40, 1432 (1907).

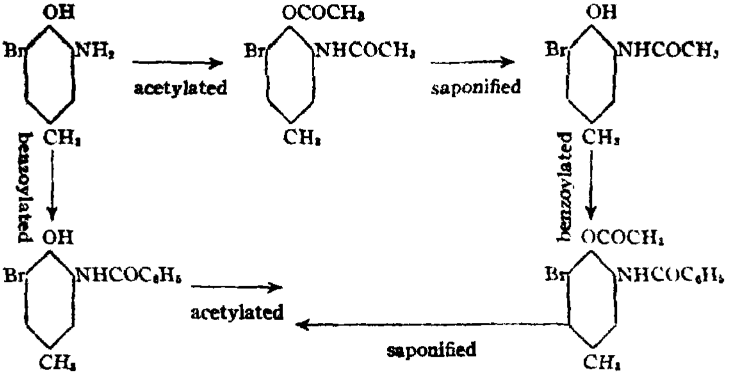
[3] *Ibid.*, 40, 2154 (1907).

[4] *Am. Chem. J.*, 23, 1 (1900).

[5] This Journal, 36, 390 (1914).

[6] *Ann.*, 311, 375 (1900).

[7] *Loc. cit.*



The suggestion[1] that the behavior of the compounds here described might be explained by the possibility that both acyl radicals were bound to nitrogen, and that the substances belong in the class known as alkali-insoluble phenols, does not seem to be in agreement with the facts. In the first place, the compounds are not insoluble in alkali solution, although the ease with which solution takes place is not the same for all cases. The fact that a diacetyl derivative dissolves (through saponification) more rapidly than the corresponding acetyl-benzoyl compound, and an unsubstituted diacyl derivative dissolves more quickly than a substituted one, could possibly be explained by steric hindrance. It should be noted, also, that the concentration of the alkali solution here used did not exceed 1% and that the reactions took place at room temperature, while that employed by Torrey and collaborators[2] and by Adams[3] in testing the solubility of alkali-insoluble phenols had a concentration of 10% and was often used at the boiling point. Moreover, Adams has shown that the insolubility in alkali of the class of so-called alkali-insoluble phenols represented by the phenylhydrazones of *o*-hydroxyaldehydes and ketones depends chiefly upon (1) the tendency of the sodium salts of these phenols to hydrolyze, (2) the extreme insolubility of the free phenols in water, (3) the temperature of the alkali solution, and (4) the increase in molecular weight brought about by the introduction of any atom or group of atoms into any part of the molecule, and not upon the structure of the compound, except in the case of the nitro derivatives. In addition to these differences, many of the alkali-insoluble phenols are highly colored, while only a few of the compounds here investigated had even a slight color and most of them were colorless. Finally, no diacylated aminophenols having both acyl radicals attached to nitrogen seem to have been recorded in the literature, and specific attempts by Tingle and Williams[1] to prepare them were unsuccessful.

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[1] Made during the discussion at the time this paper was presented in abstract at the Philadelphia meeting of the American Chemical Society, September 5, 1919.

[2] *Loc. cit.*

[3] This Journal, 41, 247 (1919).

As has been noted above, Ransom[2] found, in the diacylated aminophenols prepared in his work, that the lighter acyl radical was always attached to nitrogen, and that in the work here reported the heavier of the two acyls went to nitrogen. In comparing these results, and in trying to account for the differences, it seemed necessary to consider the fact that Ransom's work was done with *o*-aminophenol in which there were no acid-forming substituents, while two of the bases employed in my work had a part of the benzene hydrogen replaced by bromine. Recent work[3] in this laboratory, as well as the results of work done elsewhere, indicates that the reactions of a phenolic hydroxyl, or of an amino group attached to a benzene ring, may be very appreciably modified by the presence of acid-forming substituents in the ring. On this account it seemed desirable to repeat, with *o*-aminophenol, all the experiments that had been carried out with the substituted bases specified above. This was done, care being taken to duplicate conditions as far as possible in all cases. The results, however, show that the same type of migration occurred in both instances, from which it appears that the acid-forming substituents are not alone responsible for the rearrangement.

Work is in progress with bases containing other substituents, in which an attempt will be made to determine whether the rearrangement observed is dependent on the differences in weight of the radicals used, their chemical characteristics, or upon the relative positions of the hydroxyl and amino groups.

Experimental.

2-Benzoylamino-4-methyl-6-bromophenyl Acetate, $C_6H_2(OCOCH_3)(NHCOC_6H_5)CH_3.Br$.—The starting point in the preparation of this compound was *m*-nitro-*p*-cresol,[1] which was first brominated according to the method used by Thiele and Eichwede.[2] A much better yield of a purer product was obtained by a modification of Zincke and Wiederhold's method.[3] The bromination was carried out in chloroform solution, using a slight excess of bromine, in the presence of iron filings, and after allowing the mixture to stand for 48 hours the chloroform was removed by distillation. At this point Zincke and Wiederhold purified their bromine derivatives by distillation or by crystallization, according to the volatility of the product in question. In the present case it was found more satisfactory to boil the residue with ammonia water and filter, which removed the nitrobromocresol in the form of its ammonium salt and left the iron compounds in the flask. The ammonium salt was next decomposed by hydrochloric acid and the free nitro compound that separated was further purified by repeated crystallization from alcohol, from which it separated in the form of orange-colored leaflets that melted at 69°, in agreement with the observations of Thiele and Eichwede.[4] The yield of pure material was about 65%, but this may be increased very much by working up the mother liquors.

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[1] *Am. Chem. J.*, 37, 51 (1907).

[2] *Loc. cit.*

[3] Unpublished research Mr. R. L. Howard has found that the amount of phenolic ether formed by several different methods, and the extent to which such ethers can be decomposed by heating them with ammonia under pressure, may depend, to a very considerable extent, on the presence of acid-forming substituents, while Mr. R. Taft has shown that the formation of diacetanilides is accelerated by the presence of such substituents in certain positions. In both cases the ortho position seems to exert the greatest influence.

2-Amino-4-methyl-6-bromophenol, $C_6H_2OH.NH_2.CH_3.Br$.—To prepare the hydrochloride of this aminophenol, Thiele and Eichwede reduced the nitro compound mentioned above by means of stannous chloride and hydrochloric acid dissolved in glacial acetic acid, and removed the tin salt with hydrogen sulfide. In my work the reduction was carried out very quickly and the separation from tin salt effected by much less labor by following the method described by Raiford.[5] From the hydrochloride thus obtained, dissolved in water, the free base was prepared by adding a solution of ammonium carbonate. The precipitated base was filtered off at once, washed with several portions of water, and dried on clay plate, in which condition it melted at 92–3°. Crystallization from alcohol did not change the melting point.

2-Acetylamino-4-methyl-6-bromophenyl Acetate, $C_6H_2(OCOCH_3)(NHCOCH_3)CH_3.Br$.—One molecular proportion (2.5 g.) of the base described above was mixed with an equal weight of anhydrous sodium acetate and about 3 cc. (two mols.) of acetic anhydride. The mixture, which became very warm at once, was further heated over a direct flame until the whole was fluid, after which it was allowed to stand until it reached the room temperature. The crystalline solid was next triturated with enough water to dissolve the sodium acetate present, and the mixture filtered. The dried residue began to shrink at about 155° and was entirely melted at 166°. Two crystallizations from alcohol gave a product that softened at 160° and melted at 169°. A second portion was purified as follows: A hot concentrated chloroform solution of the substance in a suitable flask was placed under a reflux condenser, and the liquid raised to the boiling point. Through the condenser tube ligroin (b. p. 80–90°) was slowly dropped until the solution began to deposit crystals, after which the flask was removed and allowed to cool. This treatment gave beautiful, colorless, feathery crystals that showed signs of softening at 160° and melted sharply at 169°. This compound is soluble in other organic solvents but none gave as satisfactory crystals as the mixture named above. It dissolves readily in cold solution of sodium hydroxide[1] which saponifies it at the *o*-connection. Analysis[2] for halogen indicated a diacetyl compound.

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[1] *Ber.*, **24**, 1960 (1891).

[2] *Ann.*, **311**, 375 (1900).

[3] *Ibid.*, **320**, 202 (1902).

[4] *Loc. cit.*

[5] *Am. Chem. J.*, **46**, 419 (1911)

Subs., 0.2014; AgBr, 0.1331.
Calc for $C_{11}H_{12}O_3NBr$: Br, 27.95. Found: 28.12.

2-Acetylamino-4-methyl-6-bromophenol, $C_6H_2OH(NHCOCH_3)CH_3.Br$.—2.86 g. of the above-described diacetyl compound was shaken with 75 cc. of cold water containing 1.0 g. of sodium hydroxide until practically all solid had disappeared and the liqud had a pale yellow color. The mixture was then filtered, the clear filtrate acidified with hydrochloric acid, and the precipitate that formed immediately was filtered off, washed with water and dried. The precipitate weighed 2.17 g., which corresponded to a yield of about 89% calculated on the basis of a monoacetyl compound as the product. The crude material melts at 127–8°, and is soluble in solutions of caustic alkalies from which it is precipitated unchanged by acids, indicating the phenolic character of the substance. It is soluble in the usual organic solvents, but was best crystallized from water out of which it was deposited in long, colorless, silky needles that melted at 129°. Analysis for bromine gave the following figures, which agree with the formula for a monoacetylated compound.

Subs., 0.0889; AgBr, 0.0687.
Calc. for $C_9H_{10}O_2NBr$: Br, 32.76. Found: 32.88.

Action of Benzoyl Chloride on 2-Acetylamino-4-methyl-6-bromophenol.—0.73 g. of the monoacetylated compound described above was dissolved in a solution made up of 50 cc. of cold water and 0.15 g. (1.25 mols) of sodium hydroxide. 0.6 g. of benzoyl chloride was next added and the whole shaken until the odor of the chloride had disappeared. The colorless solid which began to precipitate immediately was finally filtered out, washed with several portions of water and dried. A quantitative yield

[1] The significance of this behavior will be discussed, along with other cases, in a future communication.

[2] I am indebted to Mr. R. L. Howard for the analysis of this and the compound next described.

was obtained. In this condition the product began to shrink at about 160° and was melted at 168°. Repeated crystallization from alcohol gave colorless fibrous-looking masses made up of very short prisms that melted at 172°. Analysis for bromine gave results that are in agreement with a formula that requires both a benzoyl and an acetyl radical and the other reactions of the compound (see below) support this view.

Subs., 0.2457; AgBr, 0.1338.
Calc. for $C_{16}H_{14}O_3NBr$: Br, 22.97. Found: 23.17.

Proof of the Structure of 2-Benzoylamino-4-methyl-6-bromophenyl Acetate.—0.7 g. of the benzoyl-acetyl compound described above was mixed with 25 cc. of water containing 0.2 g. (2.5 equivalents) of sodium hydroxide, and shaken for some minutes. It was noted that solution took place much more slowly than in the case (see above) where both acyl radicals were acetyl, and on this account the mixture was allowed to stand overnight. The slight amount of unchanged material was removed by filtration, and the clear filtrate, which was yellow in color, was acidified by hydrochloric acid. A yellowish solid that appeared much like sand upon standing was precipitated. The melting point of the crude product was about 165°, but was not sharp. The substance is readily soluble in solutions of caustic alkali, from which acids precipitate it in the unchanged condition. It is soluble also in chloroform, ether, and alcohol, but was best crystallized from 70% alcohol, from which it separated in the form of slender, fawn-colored needles that melted at 185°. This melting point, together with the other properties and the analysis given below, show that the compound under consideration cannot possibly be 2-acetylamino-4-methyl-6-bromophenol (m. p. 129°) described on page 2073. The results of the analysis for bromine are in accordance with the requirements of the formula for 2-benzoylamino-4-methyl-6-bromophenol.

Subs., 0.2002; AgBr, 0.1242.
Calc. for $C_{14}H_{12}O_2NBr$: Br, 26.12. Found: 26.39.

In order to identify further the compound just described, and to prove that the benzoyl radical in it was attached to nitrogen, a portion of 2-benzoylamino-4-methyl-6-bromophenol was prepared in accordance with the method used by Ransom[1] in which one molecule of benzoyl chloride was slowly added to an ether solution of two molecules of the aminophenol melting at 92–3° (p. 2072). After the hydrochloride of the base, which was rapidly precipitate, was filtered off, the remaining solution was allowed to evaporate spontaneously. The residue, which melted at 182–3°, was dissolved in sodium hydroxide solution, the liquid filtered and the clear filtrate acidified with hydrochloric acid. The precipitated phenol was collected on a filter, washed several times and dried. It melted sharply at 185°, and a mixture of this product and the phenolic compound obtained by saponifying the benzoyl-acetyl derivative described on page 2074 melted at the same temperature as either of them separately, 185°. In the saponified product, therefore, the benzoyl radical is bound to nitrogen.

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[1] *Am. Chem. J.*, 23, 17 (1900).

Further proof of the relationship of the product obtained by benzoylating 2-amino-4-methy-6-bromophenol and that produced by benzoylating 2-acetylamino-4-methyl-6-bromophenol was secured by acetylating the compound that resulted in the first case. 0.25 g. of the phenol prepared by Ransom's method was mixed with an equal weight of anhydrous sodium acetate and the requisite quantity of acetic anhydride, and warmed until the whole was fluid. After cooling, the product was freed from sodium acetate and crystallized from alcohol until the melting point was constant. The substance obtained melted at 170–1°, and a mixture of this and the benzoyl-acetyl derivative described on page 2074 showed no depression. This behavior shows that in the benzoylation of 2-acetylamino-4-methyl-6-bromophenol the acetyl radical migrates to oxygen while the benzoyl radical attaches itself to nitrogen.

To test further the rearrangement shown above it was thought desirable to examine the behavior of a closely related base having two bromine atoms present. Accordingly, 4,6-dibromo-*o*-aminophenol was carried through the series of experiments specified for the base already studied.

2-Acetylamino-4,6-dibromophenyl Acetate, $C_6H_2(OCOCH_3)(NHCOCH_3)Br_2$.—The starting point in the preparation of this compound was *o*-nitrophenol, which was first converted into 4,6-dibromo-*o*-nitrophenol[1] by a method which is more convenient than any heretofore published. The nitrophenol was dissolved in 5 to 6 times its weight of glacial acetic acid, after which the calculated amount (two mols.) of bromine was added at once. The mixture was allowed to stand for 48 hours, and then poured slowly, with stirring, into 7 or 8 volumes of cold water, which precipitated the brominated product. After standing for some hours the precipitated material was removed by filtration, washed with water, and dried. Crystallization from alcohol will give a pure product, but the substance employed in this work was purified in the form of its potassium salt, which was twice crystallized from water. The free nitrobromophenol, which was obtained by decomposition of the salt by hydrochloric acid, was finally crystallized from alcohol. It melted sharply at 117°, which is in agreement with the literature.

The preparation of the free base was carried out by reduction of the nitro compound and purification of the resulting aminohydrochloride as described by Raiford[2] after which the aminophenol was obtained by treatment of the water solution of the hydrochloride with solution of ammonium carbonate. The precipitated base was further purified by crystallization from dilute alcohol, and was found to melt at 91–2°, and to have the other properties specified by Holz.[1]

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[1] Korner, *Ann.*, 137, 207 (1866).

[2] *Loc. cit.*

5.3 g. of the dibromo-aminophenol mentioned above was mixed with an equal weight of anhydrous sodium acetate, and the mixture warmed with slightly more than the calculated amount of acetic anhydride necessary to acylate both the amino and the hydroxyl groups. When cold the resulting mass was extracted with enough water to dissolve the sodium acetate present, and the residue dried. The product is soluble in alcohol, chloroform, and benzene, but was best crystallized from chloroform, out of which it separated in the form of colorless, fibrous-looking masses made up of fine, hair-like needles. It shrinks slightly between 190 and 195° and melts at 199°. It dissolves readily in cold solution of sodium hydroxide on account of being saponified at the *o*-connection. Analysis for halogen gave the following results, which are in accord with a diacylated compound:

Subs., 0.2136, AgBr, 0.2304
Calc. for $C_{10}H_9O_3NBr_2$ Br, 45.56 Found 45.90

2-Acetylamino-4,6-dibromophenol, $C_6H_2OH(NHCOCH_3)Br_2$.—3.5 g. of the diacylated compound just described was shaken with 25 cc. of cold water containing two equivalents of sodium hydroxide until complete solution had taken place, after which the clear liquid was acidified with hydrochloric acid. A precipitate was formed immediately. After standing for some minutes this was collected on a filter, washed with several portions of water, and dried. It is soluble in alcohol and other organic solvents, and slightly soluble in water. Samples were crystallized both from water and from 75% alcohol, but best from the latter, from which it was deposited in tufts made up of short needles radiating from a common center, and melting at 174–5° with apparent decomposition. This compound is soluble in solution of caustic alkali, from which it is precipitated in unchanged form by acids. Holz[2] prepared a monoacetyl derivative from the base used in this work, and assigned to it the structure of my product, though he found 186° to be the melting point.

Subs., 0.2815; AgBr, 0.3410.
Calc. for $C_8H_7O_2NBr_2$ Br, 51.75 Found: 51.55.

Action of Benzoyl Chloride on 2-Acetylamino-4,6-dibromophenol.—1.5 g. of the monoacetyl compound described above was dissolved in about 50 cc. of water containing 0.25 g. (1.25 mols) of sodium hydroxide, and to this was then added 0.87 g. of benzoyl chloride, after which the whole was shaken until the odor of the chloride had disappeared. A solid which tended to collect in little balls was formed at once. After standing for some time it was filtered off, washed and dried. A quantitative yield was obtained. This compound is but slightly soluble in ligroin or ether, and could not be crystallized satisfactorily from either of them. It is more soluble in chloroform or in alcohol, and was best crystallized from the latter, from which it was deposited in short, silky needles that tended to cling together in star-like masses. After several crystallizations it melted at 195–6°. A mixture of this substance and 2-acetylamino-4,6-dibromophenyl acetate, m. p. 199°, page 2075, melts at 167–71°.[1] Analysis for bromine is in agreement with a formula that requires both an acetyl and a benzoyl radical.

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[1] *J. prakt. Chem.*, [2] 32, 69 (1885).

[2] *Loc. cit.*

Subs., 0.2379, AgBr, 0.2163

Calc. for $C_{15}H_{11}O_3NBr_2$: Br, 38.71 Found: 38.69

Proof of the Structure of 2-Benzoylamino-4,6-dibromophenyl Acetate.—0.62 g. of the benzoyl-acetyl compound indicated above was mixed with 30 cc. of water containing 0.15 g. of sodium hydroxide, and the mixture shaken for some time. Saponification took place very slowly, consequently the mixture was allowed to stand overnight. Since the reaction was not completed during this period, the mixture was filtered and the unchanged material added to a fresh portion of alkali. After 24 hours practically all solid had disappeared. This portion was filtered, and the combined filtrate, which was yellow in color, was acidified with hydrochloric acid. The phenolic compound that was precipitated was collected on a filter, washed well with several portions of water, and dried. The crude material melted between 170 and 175°. It was twice crystallized from alcohol, from which it was deposited in clusters of short, very pointed needles that radiated from a common center. These melted at 198° with apparent decomposition. The behavior indicated above shows that the hydroxyl group is free, and the analysis for bromine agrees with a formula requiring the presence of a benzoyl radical. These facts, together with the behavior of a mixture of the substance under consideration and 2-acetylamino-4,6-dibromophenol (melting point 174–5°), from which the benzoyl derivative was prepared when heated, shows that the products cannot be identical. The mixture melts with decomposition at 160–2°.

Subs., 0.2012; AgBr, 0.2038.

Calc. for $C_{13}H_9O_2NBr_2$. Br, 43.10 Found: 43.10.

In order to characterize further the hydroxyl compound described above and to prove that in it the benzoyl radical is bound to nitrogen, a small quantity of the benzoylamino compound of the base under consideration was prepared according to Ransom's[2] method. 2.66 g. of 4,6-dibromo-*o*-aminophenol was dissolved in about 25 cc. dry ether, and to this was added 0.7 g. (1/2 mol) of benzoyl chloride, and the mixture allowed to stand until the odor of the chloride had nearly disappeared. The hydrochloride of the base which had meanwhile precipitated was filtered off, and the clear ether solution allowed to evaporate spontaneously. The residue melted at 193–5°, and was probably contaminated with traces of the hydrochloride only, for dissolving it in solution of sodium hydroxide and reprecipitating it with hydrochloric acid gave a product that melted quite sharply at 198°, which is the melting point of the product obtained by saponifying the acetyl-benzoyl derivative described on page 2076. A mixture of the two products melts at 198°, which indicates identity.

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[1] It is worth while to note this behavior in passing, because in preparing the benzoyl derivative in quantity it is unnecessary to isolate 2-acetylamino-4,6-dibromophenol, as was done in this case; the benzoyl derivative can be obtained by adding benzoyl chloride directly to the solution obtained by dissolving the diacetyl compound in sodium hydroxide solution.

[2] *Loc. cit.*

The relationship of the phenolic product prepared by Ransom's method to 2-benzoylamino-4,6-dibromophenyl acetate was still further established by preparing some of the latter from the phenol. 0.2 g. of the phenol was mixed with an equal weight of anhydrous sodium acetate and the required amount of acetic anhydride, and warmed until the whole became liquid. After cooling it was separated from sodium acetate and crystallized from alcohol until the melting point was constant. In this condition it did not depress the melting point of 2-benzoylamino-4,6-dibromophenylacetate, which shows that in the benzoylation of 2-acetylamino 4,6-dibromophenol the benzoyl radical goes to nitrogen, while the acetyl radical migrates to oxygen.

In view of the fact that the results reported above are not in accord with the observations of Ransom and Ransom, and Nelson[1] it was at first thought that possibly the character of the aminophenols used might have a bearing on the case. The results recorded by the observers mentioned were all obtained through the use of an aminophenol that was unsubstituted while the first observations in my work were made with aminophenols that contained acid-forming substituents. On account of these differences it became at once a matter of interest to repeat the experiments, using the unsubstituted aminophenol employed by Ransom. It may be stated at once that the results so far obtained are the same in type for both substituted and unsubstituted bases, although the saponification of the acyl derivatives of the substituted compounds is less rapid, due, possibly to steric hindrance.

2-Benzoylaminophenyl Acetate, $C_6H_4(OCOCH_3)(NHCOC_6H_5)$.—The starting point in the preparation of this compound was 2-acetylaminophenol, first prepared by Ladenburg[2] and which was obtained for my work by the saponification of the corresponding diacetyl derivative. The product melted at 201°, and had the other properties recorded in the literature. 4.5 g. of this material was mixed with about 50 cc. of water and 1.25 molecular proportions of sodium hydroxide, and the resulting solution shaken with 25% more than the calculated quantity of benzoyl chloride until the odor of the latter had disappeared. After standing for some hours the solid that had separated was collected on a filter, washed with several portions of water, and dried. The yield was nearly quantitative. In this form the substance melted at 134–5°. Crystallization from alcohol, benzene or ligroin gave slightly pinkish colored needles that melted at 138° if heated rapidly, or at 135° if heated more slowly. The compound is practically insoluble in water, but is slowly dissolved, on account of being saponified at the *o*-connection, when allowed to stand in the cold with sodium hydroxide solution. It is interesting in this connection to note that Tingle and Williams[1] subjected 2-acetylaminophenol to benzoylation by the Schotten-Baumann method, using potassium hydroxide instead of sodium hydroxide, and mixing the substances in a different order than that specified above, and obtained a good yield of dibenzoyl-*o*-aminophenol. In this work they prepared 4 diacylated aminophenols in which the acyl radicals were different, but observed no rearrangements. The reactions of my product are confirmed by analysis[2] for nitrogen.

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[1] *Loc. cit.*

[2] *Ber.*, 9, 1524 (1876). It will be shown later that this compound can be obtained by a method which is much more easily carried out than that used by Ladenburg, and that the diacetyl derivative (which was overlooked by Ladenburg) from which it was here obtained can be prepared with much less difficulty than has been done by any previous worker. The saponification of the diacetyl compound, its homologs and certain of its derivatives will form the subject of a future report.

Subs., 0.6208; N (Kjeldahl), 0.0312 g.
Calc. for $C_{15}H_{13}O_3N$. N, 5.49. Found. 5.03.

A portion of the purified material specified above was mixed with a solution of sodium hydroxide containing 2.5 equivalents of the alkali and was allowed to stand in the cold overnight or until practically all solid had passed into solution. The mixture was then filtered and the clear filtrate acidified with hydrochloric acid, whereupon a practically colorless crystalline precipitate was thrown down. This was removed, washed well with water, and when dried on clay plate melted without further purification at 165–7°. The product was readily soluble in solution of sodium hydroxide from which it could be precipitated in unchanged form by the addition of acids, indicating its phenolic character. To show that the product in question could not be an impure specimen of the acetylaminophenol (m. p. 201°) with which the experiment was started, portions of the two products were mixed and melted. The mass began to melt at 148° and was entirely liquid at 187°. A second portion of the product obtained by saponification of the benzoyl-acetyl derivative was further purified by repeated crystallization, after which it melted sharply at 167°. This, together with the behavior already noted, showed that the product in question could not be identical with the acetylaminophenol melting at 201°.

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[1] *Loc. cit.*

[2] I am indebted to Mr J L Clark for this analysis.

To determine whether it was benzoyl-*o*-aminophenol, described by Hubner[1] and by Ransom,[2] a portion of that compound was prepared according to the directions given by Ransom, and its properties carefully compared with those of my product. They agreed in every particular, and a mixture of the products melted at the same temperature as either of them separately, 167°.

The identity of the two products was still further established by converting them into acetyl derivatives. Each was mixed with an equal weight of anhydrous sodium acetate and the requisite amount of acetic anhydride, and heated for a few minutes. After purification in the usual way, the product in each case had the melting point 134° or 138° (depending on the rate of heating) and other properties given above under 2-benzoylaminophenyl acetate. Each of the products melting at 167° was benzoylated in accordance with the Schotten-Baumann method, and each gave a product which, after crystallization from alcohol, melted at 182°. These products were melted together without depressing each other's melting point, and were found to be identical with 2-benzoylaminophenyl benzoate, reported by Kalckhoff.[3]

Summary.

1. When certain *o*-aminophenols were acylated in such a way as to introduce acetyl and benzoyl groups into the same molecule, the heavier of these radicals was found attached to nitrogen, regardless of the order in which the radicals were introduced. In one case a molecular rearrangement must have occurred.

2. So far as the work has been carried, no differences have been observed between the behavior, in this respect, of substituted and unsubstituted aminophenols, which indicates that acid-forming substituents are not responsible for the rearrangement.

3. It is recognized that factors other than the weight of the acyl radicals may determine the behavior observed in this work, and these are now under consideration

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[1] *Ann.*, **210**, 387 (1881).

[2] *Am. Chem. J.*, **23**, 17 (1900)

[3] *Ber.*, **16**, 1828 (1883).

CERTAIN METALLIC DERIVATIVES OF HYDROXY-ANTHRAQUINONES.[1]

By M. L. Crossley

Received September 25, 1919

Hydroxy-anthraquinones, such as alizarine, anthrapurpurine and flavopurpurine, form copper, cadmium, nickel and iron salts when boiled in an organic solvent with the corresponding metallic chlorides, anhydrous sodium acetate, and nitrobenzene. These compounds appear to be normal salts in which the metal has replaced hydrogen of the hydroxyl groups. Similar hydroxy-anthraquinone salts of other metals have been prepared by this method but have not yet been thoroughly investigated.

These salts are practically insoluble in cold water, but dissolve readily in methyl and ethyl alcohols as well as in acetone, from which solvents they crystallize fairly well.

Wool, when boiled in a water suspension of the copper, cadmium, cobalt, nickel, chromium and iron alizarates, is dyed a pale shade of the color which alizarine gives on wool previously mordanted with the corresponding metallic salt. The dye is evenly distributed through the fiber and appears to be as firmly held by it as in the case when produced in the mordanted fiber. This, it seems to me, is positive evidence that the color produced by alizarine or similar hydroxy-anthraquinones in mordanted fiber is a property of the corresponding normal salt of the metal whose salt was used to mordant the fiber and that it is evidence of a chemical reaction. This does not mean that the dyeing of the fiber is wholly a chemical phenomenon. Undoubtedly, physical phenomena such as surface tension, diffusion, adhesion, the colloidal state, etc., one or several, contribute to the distribution of the dye in the fiber and to its retention by it. On the one hand, Liechte and Suida, Liebermann, Guggiari[2] have expressed the opinion that the alizarine lakes have the composition of normal salts, while, on the other hand, Biltz, Haller and others,[3] think that lake formation is a phenomenon of a colloidal character. It seems to me that the evidence will not justify the conclusion that the formation of an alizarine lake is wholly a physical or a chemical phenomenon, but rather should be interpreted to mean that it is the result of the combined action of physical and chemical phenomena.

I believe the dye to be *in* the fiber and not simply *on* the fiber. Long boiling and scrubbing of the wool dyed with the sparingly soluble alizarine salts mentioned did not result in removing any more dye than was removed by similar treatment of the wool previously mordanted and then dyed with alizarine. Whatever salt entered the fiber was held as firmly as when produced in it. The fact that the color was evenly distributed through the fiber is also evidence that it was not simply on the surface.

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[1] Presented before the Organic Division of the American Chemical Society at Philadelphia, September 2–6, 1919.

[2] *Ber.*, 45, 2442 (1912).

[3] *Färber Ztg.*, 480, 523 (1912).

Experimental Part.

Copper Alizarate.—6 g of powdered C. P. alizarine, 4 g. of cupric chloride, 5 g. of anhydrous sodium acetate, and 100 cc. of nitrobenzene were boiled for 5 hours in a flask fitted with a reflux condenser. The reaction mass was allowed to cool, after which it was filtered, washed with water and then with ether and finally crystallized from methyl alcohol. The yield was 7 g.

It is a dark red substance which is insoluble in cold water and only very slightly soluble in boiling water. It dissolves readily in ethyl and in methyl alcohols, giving a wine-red solution with the former and a darker red solution with the latter. With acetone it gives a dark red solution and with nitrobenzene a dark brown. It gives a dark purple solution with aniline. It is insoluble in ether, benzene, carbon disulfide, chloroform and petroleum ether. It is decomposed by dilute mineral acids.

Calc. for $C_{14}H_6O_4Cu$ Cu, 21.08 Found 20.86.

Cadmium Alizarate.—A mixture of 3 g. of alizarine, 2.3 g. of cadmium chloride, 3 g. of anhydrous sodium acetate, and 100 cc. of nitrobenzene was boiled in a flask provided with a reflux condenser for 5 hours. The reaction mass was cooled, filtered, washed with water and with ether and then crystallized from methyl alcohol. The yield was 3 g.

It is a purplish brown product which is practically insoluble in water, ether and benzene. It is soluble in methyl alcohol, ethyl alcohol, and acetone, giving wine-red solutions. Mineral acids decompose it.

Calc for $C_{14}H_6O_4Cd$ Cd, 32 Found 32.3

Nickel Alizarate.—6 g. of alizarine, 3 g. of nickel chloride, 5 g. of anhydrous sodium acetate, and 100 cc. of nitrobenzene were boiled for 5 hours in a flask with a reflux condenser. The reaction product was poured into cold water and filtered. It was then washed with water and ether and crystallized from methyl alcohol The yield was 7 g.

It is a dark purple product which is insoluble in water. It dissolves readily in hot methyl and ethyl alcohol, giving dark red solutions. With acetone it gives a brown solution and with aniline an olive-green. It is but slightly soluble in boiling ether and benzene.

Calc for $C_{14}H_6O_4Ni$: Ni, 19.77. Found: 19.84.

Iron Alizarate.—6 g. of alizarine, 4 g. of ferric chloride, 5 g. of sodium acetate, and 100 cc. of nitrobenzene were boiled for 5 hours in a flask with a reflux condenser. The product was poured into water, filtered, and washed with ether. It was purified by crystallization from acetone. The yield was 7.6 g.

It is a dark red product, insoluble in water, quite soluble in methyl alcohol, ethyl alcohol, and acetone, giving purple solutions, but slightly soluble in ether and benzene.

Calc for $C_{14}H_6O_4Fe$ Fe, 19.05 Found 19.8

The cobalt and chromium salts of alizarine as well as the copper and nickel salts of anthrapurpurine and flavopurpurine were prepared and, with the exception of the cobalt salt of alizarine, which analyzed for $C_{42}H_{21}O_{12}Co$, appear to be normal salts.

Summary.

Copper, cadmium, nickel and iron salts of alizarine are formed when alizarine is boiled with the respective salts of these metals, anhydrous sodium acetate, and nitrobenzene.

These alizarine salts, though slightly soluble in water, penetrate unmordanted wool fiber and produce colors identical with those produced by alizarine in wool fibers mordanted with the respective metallic salts. These dyes appear to be *in* the fiber and not simply *on* the fiber.

The formation of an insoluble alizarine dye in a mordanted fiber is accomplished by the combined action of physical and chemical phenomena.

BOUND BROOK N J

GENTIAN VIOLET—ITS SELECTIVE BACTERICIDAL ACTION.[1]

BY M L CROSSLEY

Received September 25, 1919

Shortly after the United States entered the war, it was discovered that the supply of gentian violet dye used in biological work as a differentiating stain was limited. Prior to the war, this material had been imported from Germany and no particular attention had been given to its composition. Careful study of the available literature gave no information of importance and it was decided to undertake an investigation of the product in order to determine its composition. Some of the information found in the literature was later discovered to be erroneous or confusing. For example, Pappenhein[2] states that it belongs to the rosaniline group and probably contains dextrine. This fact proved to be correct. On the other hand, Muhr and Richie[3] consider it synonymous with benzyl violet and pyoktanin. This, of course, is an erroneous judgment, for benzyl violet is a mixture of benzyl-pentamethyl-*p*-rosaniline hydrochloride and hexamethyl-*p*-rosaniline hydrochloride, while pyoktanin is a trade name for a mixture of hexamethyl-*p*-rosaniline hydrochloride and pentamethyl-*p*-

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[1] Presented before the Dye Section of the American Chemical Society at the Philadelphia meeting, September 2–6, 1919.

[2] *Grundriss der Farb Chemie zum Gebrauch bei Mikroskopischen Arbeiten.*

[3] "Manual of Bacteriology," p. 101.

rosaniline hydrochloride. Pyoktanin then is another name for methyl violet B.

A preliminary study of the gentian violet obtained from the Grübler laboratory at Leipzig, furnished me by the Connecticut State laboratory, showed the product to be mixture of dextrine and dye in about equal proportions. A qualitative study of the physical and chemical properties of the dye indicated that it belonged to the triphenylmethane class and that it contained free amino hydrogen. Further investigation showed that the dye was chiefly a mixture of hexamethyl-*p*-rosaniline hydrochloride and pentamethyl-*p*-rosaniline hydrochloride.

On acetylation of the dye, two products were obtained: one which did and one which did not contain an acetyl group. The first was a violet dye which reduced to a product identical with hexamethyl-*p*-leucaniline; the other reduced to acetyl-pentamethyl-*p*-leucaniline. The limited quantity of material available for the investigation and the difficulty encountered in making a sharp separation of the two products made it impossible to get a quantitative analysis of the product. The sample investigated, however, showed that hexamethyl-*p*-rosaniline hydrochloride was present in larger proportion than the pentamethyl product. There was also present a small amount of another dye which gave an acetyl derivative not crystallizable from the acetic acid solution and which, on reduction and qualitative study, appeared to be the acetyl derivative of the tetramethyl-*p*-rosaniline hydrochloride. It would, therefore, appear that the so-called gentian violet is simply a prepared mixture or blended mixture of the above mentioned dyes.

In view of the fact that Dr. Churchman had shown gentian violet to possess selective bactericidal action, and since it now appeared that gentian violet was not an individual dye, it, therefore, seemed pertinent to learn whether or not the selective activity of gentian violet was an inherent property of the mixture called gentian violet or of one or both of its components. Using the method suggested by Dr. Churchman,[1] it was found that the organisms which are destroyed by gentian violet in the dilution of 1 : 100,000 parts, were also destroyed by hexamethyl-*p*-rosaniline hydrochloride, pentamethyl-*p*-rosaniline hydrochloride and rosaniline in the same dilution, and those that were negative to gentian violet were also negative to the other dyes mentioned. For example, *B. Prodigiosus*, *B. fluorescens* (liquefying and non-liquefying), *B. mucosus capsulatus* or pneumobacillus of Friedländer, *Streptococcus pyogenes* and *B. coli* (*communis*), grew equally well on agar agar medium containing gentian violet, hexamethyl-*p*-rosaniline hydrochloride, pentamethyl-*p*-rosaniline hydrochloride and rosaniline in the dilution of 1 : 100,000, while *B. subtilis*, *B. cereus*, *Sarcina aurantiacea*, *Sarcina lutea*, *Staphylococcus*

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[1] *J. Exp. Med.*, 16, 228–248 (1912); 18, 579–583 (1913).

pyogenes, *B. violaceae* and *B. mycoides* were killed by all 4 compounds in the dilution of 1 : 100,000 It is, therefore, evident that the selective bactericidal action of gentian violet was a property of its components. That this selective action is related to the constitution of the dye, I have no doubt. It seems that the effectiveness of any one of the dyes mentioned in killing organisms is governed by two factors; first, the composition of the dye, and second, the nature of the organism. Both chemical and physical phenomena are undoubtedly concerned in the reaction.

Malachite green will kill *B. subtilis* and *B. mycoides* in the dilution of 1 : 100,000, but not in the dilution of 1 : 200,000. In fact, no one of the dyes mentioned is effective for *B. subtilis* in dilutions greater than 1 : 100,000. *B. mycoides*, however, is destroyed by malachite green in the dilution of 1 : 100,000, rosaniline in dilution of 1 : 200,000, and by gentian violet, hexamethyl-*p*-rosaniline hydrochloride, and pentamethyl-*p*-rosaniline hydrochloride in the dilution of 1 : 300,000. The constiution of the dye is, therefore, and important factor.

It would seem from the evidence at hand, that this selective bactericidal action of the dyes mentioned is a property of the triphenylmethane dyes and is particularly related to the basic nitrogen groups. An increase in the number of these groups and substitution of methyl radicals for amino hydrogen seem to intensify the bactericidal power. This suggests an extremely interesting and important line of research, that is, the relation of chemical constitution to selective bactericidal action. I feel, however, that this problem cannot be successfully attacked from the chemical point of view only. In order to understand the chemistry involved, we must know more about the composition of bacteria. I am inclined to believe that the part played by the bacteria in this selective action is of prime importance.

Of the group of organisms studied, those that were gram positive, that is, those that were stained by the dye, were also gentian positive, that is, killed by gentian violet; while those that were gram negative were not inhibited in their growth by gentian violet. This same observation was true with respect to the other dyes mentioned. This, it seems to me, is evidence of a chemical reaction between some component or components of the bacteria cell and the dye. It has already been shown[1] that malachite green combines with sodium nucleate to form a black, porous nucleate of the dye. This selective bactericidal action seems then to be caused by the presence of compounds with reactive groups in the structure of the bacteria capable of readily combining with the dyes mentioned through certain reactive groups in their structure. Wherever this combination results in the formation of compounds which are detrimental to the life functions of the organisms, either limitation or complete destruction of their life activities result.

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[1] *Biochem. Z.*, **42**, 440–469 (1912).

I believe that careful investigation will show that there is variation of the susceptibility of bacteria to different chemical destructive agents and that no one chemical substance is capable of destroying all species of bacteria. There is then much work to be done in this field, for the whole system of sanitation rests upon the assumption that a disinfectant capable of killing certain pathogenic organisms will generally kill others. I trust that some biological chemist will take up this problem and continue the investigation, since I am no longer in a position to do so.

Experimental Part.

1. **Alcohol-insoluble Portion of Gentian Violet.**—2.2285 g. of the Grübler gentian violet was extracted with absolute alcohol and filtered. The residue was washed with alcohol until the filtrate was colorless. It was then dried and weighed. 1.1124 g. was obtained. This represented 49.92% of the dye. A second analysis gave 49.54% of alcohol-insoluble material. This product was soluble in water, gave the iodine test for dextrine, gave a brown solution with sulfuric acid which charred on heating and gave the characteristic dextrine odor. A water solution of the product reacted with an ammoniacal solution of lead acetate to give a heavy, white precipitate. The water solution had the characteristic dextrine odor. This evidence proved the alcohol-insoluble substance to be dextrine.

2. **Ash.**—0.6140 g. of dye was ignited in a platinum crucible and 0.0070 g. of ash, equal to 1.14% obtained.

3. **Identification of the Dye.**—The alcohol solution of the dye was carefully evaporated to dryness and dried to a constant weight. It was soluble in water and the solution gave the following reactions: It reacted with a solution of picric acid to give an insoluble, dark violet picrate; it gave a dark brown precipitate when treated with sodium hydroxide; it reduced to a colorless solution when treated with ammonium hydroxide and zinc dust, and gave an insoluble red-violet precipitate when treated with potassium dichromate solution. The dye dissolved in conc. sulfuric acid giving an orange colored solution which on dilution with water changed to red-green, then to green, to blue, and finally to violet, with increasing dilution, color phenomena characteristic of the alkylated *p*-rosanilines. When a portion of the dye was boiled with anhydrous sodium acetate and an excess of acetic anhydride, a solution was obtained which gave a violet spot with a green ring indicating the presence of free amino hydrogen in the dye. This evidence indicated that the dye belonged to the *p*-rosaniline group and confirmed Pappenheim's opinion. This was proven as follows: A portion of the dye was mixed with an excess of acetic anhydride and anhydrous sodium acetate and boiled several hours. The reaction product

was dissolved in water and salted with sodium chloride and zinc chloride. A violet precipitate formed leaving a green solution. This was filtered and the violet dye again dissolved in water and again salted with sodium chloride. The resulting dye was filtered and the filtrate added to that obtained from the previous filtration. The violet dye was then reduced and gave a product melting at 173°, proving it to be hexamethyl-*p*-leucaniline which showed that the violet dye was hexamethyl-*p*-rosaniline hydrochloride. The green solution was reduced with zinc dust and gave a precipitate of a leuco compound which crystallized from pure alcohol as colorless, concentric, needle crystal aggregates, melting at 142-3°. It analyzed for $C_{26}H_{31}N_3O$ and was identical with acetyl-pentamethyl-*p*-leucaniline.

Calc. for $C_{26}H_{31}N_3O$· N, 10 47. Found: 10.32.

This was treated with hydrochloric acid and converted into a substance crystallizing from dilute alcohol in colorless needles. From benzene the substance crystallized in beautiful, colorless coalescent spears, melting at 115 to 116°. It analyzed for $C_{24}H_{29}N_3$ and was pentamethyl-*p*-leucaniline.

Calc. for $C_{24}H_{29}N_3$. N, 11.7. Found: 11.83.

By oxidation of this a beautiful violet dye was obtained which was evidently pentamethyl-*p*-rosaniline. The filtrate from the acetyl-pentamethyl-*p*-leucaniline gave on standing a small quantity of a product which appeared to be an acetyl-tetramethyl-*p*-leucaniline. The small quantity available made a thorough study of it impossible. It would, therefore, seem that gentian violet is chiefly a mixture of hexamethyl-*p*-rosaniline and pentamethyl-*p*-rosaniline hydrochlorides with probably a small quantity of the tetramethyl product.

4. The Selective Bactericidal Action of Gentian Violet and its Compounds.—Several organisms which had previously been shown to be gentian positive and gentian negative were selected and the method of Churchman adopted for a study of their behavior with gentian violet free from dextrine, and C. P. samples of the dyes found in gentian violet. In order to see if the alkyl groups in these dyes had any important influence on their bactericidal properties, rosaniline was selected for comparative study. Malachite green was also used to study the effect of the number of basic nitrogen groups. The investigation was only preliminary and by no means exhaustive.

Divided plates of agar agar medium, one-half dyed with dye solution, were made as suggested by Churchman and the organisms under investigation planted on the undyed portion. Series A represents gentian violet free from dextrine, dilution 1 : 100,000; series B, hexamethyl-*p*-rosaniline hydrochloride, dilution 1 : 100,000; series C, pentamethyl-*p*-rosaniline hydrochloride, dilution 1 : 100,000; series D, rosaniline, and series E, the above mentioned substances and malachite green in different dilutions. The organisms reported in the corresponding tables as gentian positive did not grow across into the dyed portion of the plates, while those indicated as negative did. It will be observed that in dilutions of 1 : 100,000 there was no difference in the effectiveness of the dyes for the organisms selected. With greater dilutions the bactericidal power of the dyes for two gentian positive organisms diminished with the decreasing number of the methyl groups and the basic nitrogen groups. It will be seen from Table E that rosaniline was more effective for *B mycoides* than malachite green. In other words 3 unsubstituted amino groups were more effective than 2 in which the 4 hydrogens had been substituted by methyl radicals. Comparing the effectiveness for *B mycoides* of the 4 substances up to a dilution of 1 300,000 it will be seen that hexa- and pentamethyl-*p*-rosaniline appear equal in strength and that they are the most effective of the group

TABLE I —SERIES A

Gentian Violet free from Dextrine Dilution 1 100,000

Gram + = retains stain Gentian + = inhibited

Gram — = does not retain stain Gentian — = not inhibited.

Organism	Gram + or —	Gentian + or —
B Prodigiosus	—	—
B Subtilis	+	+
B Cereus	+	+
B Fluorescens (liq)	—	—
Sarcina Aurantiaca	+	+
B Mucosus Capsulatus or Pneumobacillus of Friedlander	—	—
Sarcina Lutea	+	+
Streptococcus pyogenes	—	—
Staphylococcus pyogenes	+	+
B Coli (communis)	—	—
B Violaceae	+	+
B Fluorescens (non-liq)	—	—
B Mycoides	+	+

TABLE II —SERIES B

Hexamethyl *p* rosaniline Hydrochloride Dilution 1 100 000

Organism	Gram + or —	Gentian + or —
Sarcina Lutea	+	+
B Fluorescens (liq)	—	—
Sarcina Aurantiaca	+	+
B Violaceae	+	+
B Mucosus Capsulatus	—	—
B Prodigiosus	—	—
B Cereus	+	+
B. Mycoides.	+	+
B. Fluorescens (non-liq)	—	—
B. Subtilis	+	+

Table III.—Series C

Pentamethyl-*p*-rosaniline Hydrochloride Dilution 1 100000

Organism	Gram + or −	Gentian + or −
Sarcina Lutea	+	+
B Fluorescens (liq)	—	—
Sarcina Aurantiaca	+	+
B Violaceae	+	+
B Mucosus Capsulatus	—	—
B Prodigiosus	—	—
B Cereus	+	+
B Mycoides	+	+
B Fluorescens (non liq)	—	—

Table IV.—Series D

Rosaniline Dilution 1 100000

Organism	Gentian + or −
Sarcina Lutea	+
B Fluorescens (liq)	−
Sarcina Aurantiaca	+
B Violaceae	+
B Mucosus Capsulatus	—
B Prodigiosus	—
B Subtilis	+
B Fluorescens (non liq)	—
B Mycoides	+

Table V.—Series F

Different Concentrations of Dyes

Organism	Dyes					Dilution
	G V	Hexa	Penta	Rosa	Mola	
B Subtilis	+	+	+	+	+	1 100000
B Subtilis	—	—		—	—	1 200000
B Mycoides	+	+	+	+	+	1 100000
B Mycoides	+	+	+	+	+	1 200000
B Mycoides	+	+	+	−	—	1 300000
B Mycoides			—	−	−	1 400000

Each of the organisms was also studied with respect to its behavior with the gram stain and the result in each case was the same. All the gram positive organisms were gentian positive

Summary.

1. Gentian violet is a mixture of dextrine and dye in about equal proportions. The dye is a mixture chiefly of hexamethyl-*p*-rosaniline hydrochloride and pentamethyl-*p*-rosaniline hydrochloride with small quantities of lower homologs, particularly the tetramethyl compound.

2. The selective bactericidal action of gentian violet is no greater than that of its component dyes and gentian violet has no advantage over these in selective or differentiating power.

3. The organisms found to be gentian positive were also gram positive, indicating that both the structure of the dye and that of the organism

are important factors in the selective action. The organisms that are positive fix the dye because they possess compounds in their structure capable of reacting with the dye to form new complexes which limit or destroy the cell activity of the organism. The concentration of the dye is an important factor in determining its power to kill the organism, or in other words, the survival of the organism depends upon the degree to which the destructive reaction between its components and the dye has taken place and this in turn is dependent on the amount of dye which the cell has absorbed.

4. The effectiveness of the dyes used was the same in dilutions of 1 : 100,000 but different in greater dilutions.

5. No one of the dyes was effective for *B. subtilis* in dilutions greater than 1 : 100,000. *B. mycoides* was killed, however, by malachite green in dilution of 1 : 100,000, by rosaniline in dilution of 1 : 200,000, and by gentian violet, pentamethyl- and hexamethyl-*p*-rosaniline hydrochloride in a dilution of 1 : 300,000.

6. The basic nitrogen groups appear to be the reactive groups and their action is intensified by substitution of methyl for amino hydrogen.

I am greatly indebted to Mr. John Burisch, formerly a student at Wesleyan University, for assistance in the bacteriological part of this investigation, and hereby express my deep appreciation of his valuable work.

BOUND BROOK, N. J.

[CONTRIBUTION FROM THE LABORATORIES OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH.]

SYNTHESES IN THE CINCHONA SERIES. II. QUATERNARY SALTS.

BY WALTER A JACOBS AND MICHAEL HEIDELBERGER.

Received October 1, 1919.

In a recent communication a plan was outlined for the synthesis of aromatic arsenic compounds for biological study.[1] The present paper and that following it represent an attempt to apply a similar method of treatment to the field of the cinchona alkaloids, whose possibilities as material for chemotherapeutic study in one direction have been shown by the remarkable specificity for the pneumococcus displayed by ethylhydrocupreine.[2]

Without entering into any extended discussion it may be stated that previous synthetic studies in the cinchona group have consisted mainly in the preparation of ethers of the phenolic hydroxyl group at (1) in the formula (ethylhydrocupreine being the ethyl ether), and in the formation of a large variety of esters, making use of the alcoholic hydroxyl group (2), many of the latter substances having been produced in the search for a tasteless quinine derivative.

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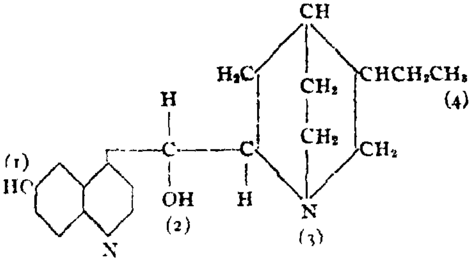
[1] THIS JOURNAL, 41, 1581 (1919).

[2] Morgenroth and Levy, *Berl. klin. Wochschr.*, 48, 1560, 1979 (1911).



Several years ago the writers made an extended study of the quaternary salts of hexamethylene-tetramine, many of which proved to possess considerable bactericidal power.[1] Since the cinchona alkaloids also contain a reactive tertiary amine group at (3) it was thought possible that from these also bactericidal or, more specifically, pneumococcidal substances might be synthesized using this as a basis. The present paper gives the chemical part of the work, and the bacteriological and biological findings will be reported in the appropriate place by Dr. Martha Wollstein, who has had charge of this phase of the work.

The methochlorides are, of course, the simplest quaternary salts possible, and a number of these were prepared as a basis for comparison. Next in complexity come the benzyl chlorides, several of which were obtained crystalline for the first time. Another larger, new group consisted of the salts formed with the chloroacetyl derivatives of ammonia, the lower aliphatic amines, and of benzylamine. Up to this point the salts were in general fairly readily soluble in water and in dilute solution did not give precipitates with alkali. In the case of the chloroacetyl derivatives of the aromatic amines the new series of salts with the alkaloids were only sparingly soluble in cold water, and were, therefore, converted into their water-soluble hydrochlorides in order to render them suitable for biological testing. The aqueous solutions so obtained gave precipitates of the quaternary bases on making alkaline with sodium hydroxide, but in only one case was a crystalline base obtained. The quaternary salts with the aromatic chloroacetyl derivatives also dissolved in dil. nitric acid, most of them soon depositing beautifully crystalline, sparingly soluble dinitrates or chloride nitrates, a representative of each group being described and analyzed. Most of the salts prepared crystallized with water of crystallization, or in cases in which anhydrous solvents were used, came to final equilibrium in the air with water of crystallization. Solutions of all of the salts, aliphatic as well as aromatic, yielded immediate precipitates with solutions of picric acid or potassium dichromate. The salts of alkaloids in which the side-chain at (4) had been hydrogenated and with halides containing no readily oxidizable group, also gave purple precipitates with potassium permanganate.

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[1] *J. Biol. Chem.*, 20, 659, 685 (1915); 21, 103, *et seq.* (1915); *J. Exp. Med.*, 23, 563, *et seq.* (1916).

Experimental.

The quaternary salts of the alkaloids with the chloroacetyl derivatives of the aliphatic and aromatic amines were prepared by boiling equimolecular amounts of the components in dry acetone for 5 to 7 hours, and this method is to be assumed below unless another is given. Unfortunately, no general method can be given for the isolation and purification of the salts, for although many either crystallized directly from the reaction mixture or remained as a crystalline residue when this was evaporated, most of the salts required different treatment in each case. Water of crystallization was determined in all cases after allowing the salt to come to equilibrium in the air; the water was then driven off *in vacuo* over sulfuric acid at room temperature, 80°, or 100°, depending on the properties of the salt. In the case of the hydrochlorides of the quaternary salts, most of those which were recrystallized from an aqueous solvent were first air-dried; all were dried for analysis to constant weight *in vacuo* at room temperature over sulfuric acid and crushed alkali. Nitrogen was usually determined by the Dumas method, although accurate values were also obtained by proper use of the Kjeldahl method. Halogen was determined in the majority of cases by the Volhard method, and it was sometimes necessary, owing to the formation of difficultly soluble nitrates which occasionally separated as gums before crystallizing, to add a definite excess of the silver nitrate solution and heat on the water bath before proceeding with the analysis. Optical rotations were calculated by means of the formula: $[\alpha] = \alpha \times 100/l \times c$, taking c as g. of substance per 100 cc. solvent, a close approximation for low concentrations. Melting points above 140° were corrected to the short-stem thermometer basis.

(A) Quaternary Salts of Cinchonine.

Cinchonine Methochloride.—Although this salt is mentioned in the literature[1] it does not seem to have been described. 16.8 g. of cinchonine methiodide were suspended in water and shaken for two hours with freshly precipitated silver chloride. The mixture was warmed on the water bath, filtered hot, and the filtrate treated with sodium chloride, causing the gradual deposition of the salt, which was recrystallized from water, forming rhombic crystals containing one molecule of water of crystallization. The yield was 9 g. When rapidly heated to 265°, then slowly, the air-dry or anhydrous chloride decomposes at 270°, with preliminary darkening. It dissolves readily in methyl or ethyl alcohol, less easily in water, and is almost insoluble in acetone. In water $[\alpha]_D^{20.5}$ is $+225.1°$, $c = 1.482$. The taste is weakly bitter.

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[1] Stahlschmidt, *Ann.*, 90, 219 (1854); Rosenstein, *Compt. rend.*, 130, 753 (1900).

Subs. (air-dry), 0.6863: loss, 0.0344 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{20}H_{25}ON_2Cl.H_2O$: H_2O, 4.97. Found: 5.01.
Subs. (anhydrous), 0.2432. AgCl, 0.1012.
Calc. for $C_{20}H_{25}ON_2Cl$: Cl, 10.28. Found. 10 29

Cinchonine Benzyl Chloride.—Equimolecular amounts of cinchonine and benzyl chloride were boiled daily on the water bath with acetone for about two weeks. Although considerable cinchonine remained unattacked this method avoided the partial decomposition occurring when alcohol is used.[1] The mixture was finally chilled, filtered, and the precipitate boiled with water, filtering hot. The chloride crystallized on cooling as minute rods containing no water of crystallization and melting and decomposing to a purple mass at about 280°, with preliminary darkening. Claus and Treupel give the decomposition point as 248°. The salt dissolves in hot water or alcohol, sparingly in hot acetone or chloroform, or in the cold in water or alcohol. $[\alpha]_D^{22}$ in water $= +164.8°$, $c = 0.716$.

Subs., 0 2563: AgCl, 0 0870
Calc. for $C_{26}H_{29}ON_2Cl$ Cl, 8.43 Found 8.40.

Cinchonine Iodoacetamide, $C_{19}H_{22}ON_2.ICH_2CONH_2$.—15 g. of cinchonine were dissolved in boiling alcohol and treated with 9.3 g. of iodoacetamide. After letting cool the solution was partially concentrated *in vacuo*, let stand overnight, and filtered from the precipitate of unchanged cinchonine. The filtrate, concentrated almost to dryness on the water bath, crystallized on rubbing with water, yielding 16 g. of the crude iodide. Recrystallized from water with the aid of boneblack it forms aggregates of long, thin plates and flat, prismatic needles containing 2 molecules of water of crystallization. The anhydrous salt gradually softens above 145° to a yellow jelly which darkens as the temperature is raised and decomposes slowly at about 190°. It is very easily soluble in methyl or ethyl alcohol and dissolves readily in hot water and sparingly in the cold.

Subs. (air-dry), 0.6344· loss, 0 0414 *in vacuo* at 100° over H_2SO_4
Calc. for $C_{21}H_{26}O_2N_3I.2H_2O$. H_2O, 6.99. Found: 6 53.
Subs. (anhydrous), 0.1403. 10.6 cc. N. (29.0°, 761 mm.). Subs., 0.1641: AgI, 0 0778.
Calc. for $C_{21}H_{26}O_2N_3I$ N, 8 77, I, 26 48 Found: N, 8 56; I, 25.62.

Cinchonine Chloroacetamide.—14.5 g. of cinchonine iodoacetamide were converted into the chloro compound and this isolated exactly as in the case of the methochloride. The product was recrystallized from a small volume of water, separating as rosets of minute, narrow platelets containing two molecules of water of crystallization, and melting with effervescence at 110–20° when rapidly heated. The yield was 9 g. The anhydrous chloride gradually melts to a yellow jelly when heated and liquefies completely at about 195°, with darkening and slow gas evolution. $[\alpha]_D^{25}$ in water is $+174.2°$, $c = 1.163$. It dissolves readily in water, methyl or ethyl alcohol, or chloroform, and softens under dry acetone, dissolving with difficulty. The air-dry chloride dissolves rather sparingly in cold water, a suspension clearing on adding sodium hydroxide.

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[1] Claus and Treupel, *Ber.*, 13, 2294 (1880)

Subs. (air-dry), 0.8162 loss, 0.0698 *in vacuo* at 100° over H_2SO_4
Calc for $C_{21}H_{26}O_2N_3Cl.2H_2O$ H_2O, 8.51 Found· 8.55
Subs. (anhydrous), 0.1513 14.3 cc N (23.0°, 753 mm.)
Subs., 0.1784 9.01 cc $AgNO_3$ soln (1 cc = 0.001812 g Cl)
Calc for $C_{21}H_{26}O_2N_3Cl$ N, 10.84, Cl, 9.15 Found N, 10.80, Cl, 9.15

An attempt was made to prepare the substance directly from cinchonine and chloroacetamide in boiling acetone but little ionized halogen was formed.

(B) Quaternary Salts of Cinchonidine.

Cinchonidine Methochloride.—This substance was prepared and isolated in the same way as its cinchonine stereoisomer, except that it was necessary to saturate the solution with salt after removal of the silver iodide. The crude product was sucked as dry as possible, dissolved in absolute alcohol, filtered from sodium chloride, and cautiously precipitated by the addition of dry ether A repetition of the purification process proved to be necessary. The salt forms minute needles containing between one and 1.5 molecules of water of crystallization. The test for alcohol of crystallization was negative. When rapidly heated to 230°, then slowly, the anhydrous compound melts and decomposes at 232–3° with slight preliminary softening $[\alpha]_D^{22}$ in water is $-142.7°$, $c = 1.489$. The air-dry salt begins to melt about 20° lower than the dried portion. Claus and Bock[1] give 158° as the melting point of the anhydrous salt. It dissolves readily in the cold in water, methyl or ethyl alcohol, or chloroform, and only sparingly in dry acetone.

Subs (air-dry), 0.6458 loss, 0.0394 *in vacuo* at 100° over H_2SO_4
Calc for $C_{20}H_{25}ON_2Cl.H_2O$ H_2O, 7.27 Found 6.10.
Subs (anhydrous), 0.2441. AgCl, 0.1031
Calc for $C_{20}H_{25}ON_2Cl$ Cl, 10.28. Found 10.44

Cinchonidine Chloroacetamide, $C_{19}H_{22}ON_2.ClCH_2CONH_2$.—15 g. of cinchonidine were dissolved in warm chloroform and treated with 9.5 g. of iodoacetamide, warming until clear. The next day about one-half of the chloroform was evaporated off and the iodide precipitated by means of dry ether. The crude product showed no tendency to crystallize and was accordingly dissolved in hot alcohol, diluted with water until just faintly turbid, and converted into the chloride with freshly precipitated silver chloride. The filtrate was concentrated to dryness *in vacuo*, evaporated down twice with absolute alcohol *in vacuo*, and finally taken up in

[1] *Ber.*, 13, 2191 (1880)

absolute alcohol and fractionally precipitated with dry ether. The first gummy portions were discarded until finally a white, solid, amorphous product was precipitated. This was filtered off, washed with dry ether, and dried, the yield being 3.5 g. When heated it gradually softens and turns yellow, becoming completely fluid at about 190°. $[\alpha]_D^{22.5}$ in water is —112.5°, c = 1.422. The salt dissolves readily in water, methyl or ethyl alcohol, or chloroform, and forms a gum under dry acetone, dissolving with difficulty.

Subs 0.1416: 13.3 cc N (24.5°, 755 mm)
Subs. 0.1720. 8.59 cc $AgNO_3$ soln (1 cc = 0.001812 g Cl)
Calc for $C_{21}H_{26}O_2N_3Cl$ N, 10.84; Cl, 9.15 Found: N, 10.72, Cl, 9.05

(C) Quaternary Salts of Quinine.

Quinine Methochloride.—20.5 g. of quinine methiodide were converted into the chloride in the usual manner, salting out the compound by means of sodium chloride solution. After recrystallization from absolute alcohol, 11.6 g. of the methochloride were obtained as delicate needles containing two molecules of water of crystallization. A test for alcohol of crystallization was negative. The anhydrous salt melts partially at 170–5°, liquefying completely at 196–8° to an orange fluid filled with bubbles. $[\alpha]_D^{20}$ = —211.7° in water, c = 0.655. The salt is sparingly soluble in cold water, readily on heating, and dissolves freely in alcohol and very easily in methyl alcohol. Claus and Mallmann[1] describe the methochloride as needles containing one molecule of water of crystallization, melting at 181–2° when dry, and dissolving readily in water.

Subs. (air-dry), 0.7396: loss, 0.0642 *in vacuo* at 100° over H_2SO_4
Calc for $C_{21}H_{27}O_2N_2Cl.2H_2O$ H_2O, 8.77 Found: 8.68
Subs. (anhydrous), 0.2578 AgCl, 0.0986
Calc. for $C_{21}H_{27}O_2N_2Cl$: Cl, 9.46 Found 9.46.

Quinine Benzyl Chloride.—17 g. of quinine were dissolved in warm acetone and allowed to stand in a warm place with 6.3 g. of benzyl chloride, adding acetone from time to time as it evaporated. After about a week a test portion cleared completely on dilution with water and addition of acid. Most of the acetone was then boiled off and absolute alcohol added. On warming and adding several volumes of dry ether crystallization of the salt commenced. The yield was 19.1 g. Recrystallized from absolute alcohol the chloride forms faintly yellow, rhombic prisms containing one molecule of water of crystallization. A test for alcohol of crystallization was negative. When rapidly heated to 180°, then slowly, the air-dry or anhydrous salt melts and darkens at 183–8°. $[\alpha]_D^{22}$ of the anhydrous compound in water is —230.5°, c = 1.479. The chloride has a bitter taste and dissolves freely in cold water, methyl or ethyl alcohol, or acetone; less easily in ethyl acetate, and sparingly in chloroform. Mazzara and

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[1] *Ber.*, 14, 76 (1881).

Possetto,[1] who prepared the salt in alcoholic solution, describe it as amorphous.

Subs. (air-dry), 0.8335: loss, 0.0295 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{27}H_{31}O_2N_2Cl.H_2O$: H_2O, 3.84. Found: 3.54.

Subs. (anhydrous), 0.1311: 7.4 cc. N (23.5°, 749 mm.). Subs., 0.2668: AgCl, 0.0844.

Calc. for $C_{27}H_{31}O_2N_2Cl$: N, 6.22; Cl, 7.87. Found: N, 6.40; Cl, 7.83.

Quinine Iodoacetamide.—After about 1.5 hours an acetone solution of 16.2 g. of quinine and 9.3 g. of iodoacetamide at room temperature began to deposit the quaternary salt as rhombic crystals, 22.8 g. being obtained Recrystallized from water it first softens to a paste, and separates as prisms containing 1.5 molecules of water of crystallization. In this form the iodide dissolves readily in methyl or ethyl alcohol or acetone, and is sparingly soluble in cold water, readily in hot. The anhydrous salt gradually darkens and forms a jelly when heated, finally melting completely at 175–80°. It dissolves readily in chloroform and shows $[\alpha]_D^{23} = -152.2°$ in water, $c = 1.009$.

Subs. (air-dry), 0.4789 loss, 0.0257 *in vacuo* at 100° over H_2SO_4

Calc for $C_{22}H_{28}O_3N_3I.1.5H_2O$ H_2O, 5.04 Found 5.37

Subs (anhydrous), 0.1962: AgI, 0.0898.

Calc for $C_{22}H_{28}O_3N_3I$: I, 24.93. Found. 24.73

Quinine Chloroacetamide.—20 g. of the iodide were shaken in water for two hours with excess silver chloride, warmed, and filtered. The filtrate was concentrated to dryness *in vacuo*, taken up twice in absolute alcohol and concentrated as before, and finally dissolved in absolute alcohol and cautiously precipitated by the addition of dry ether. The solid, amorphous precipitate was collected, ground up under dry ether, filtered again, and dried, the yield being 11.8 g. The chloride gradually softens above 160° and appears completely fluid at 190°, with gas evolution. $[\alpha]_D^{25}$ in water is $-159.6°$, $c = 1.473$. The salt dissolves readily in water, methyl or ethyl alcohol or chloroform, and only sparingly in acetone. On boiling an aqueous solution with sodium hydroxide ammonia is evolved.

Subs. 0.1387: 12.45 cc N (24.5°, 768 mm.). Subs. 0.2321: AgCl, 0.0787.

Calc. for $C_{22}H_{28}O_3N_3Cl$. N, 10.06; Cl, 8.49. Found: N, 10.41; Cl, 8.39.

Quinine Chloroacetanilide (Quinine Acetanilide Chloride), $C_{20}H_{24}O_2N_2.ClCH_2CONHC_6H_5$.—The method given at the beginning of the "Experimental Part" was used, with 8.5 g. of chloroacetanilide.[2] After boiling off the acetone dry chloroform was added to the already partially crystalline residue. After letting stand 19 g. of silky needles of the quaternary salt were obtained. It was purified by dissolving in absolute alcohol, filtering with the aid of boneblack, and adding several volumes of dry ether, separating after rubbing or seeding as rosets of delicate needles, which are quite hygroscopic until dried. When rapidly heated to 220°, then slowly, the salt darkens slightly above 190° and melts with decomposition at 224–5°. $[\alpha]_D^{23.5}$ in absolute alcohol is —131.5°, c = 1.046. It dissolves readily in methyl or ethyl alcohol, sparingly in dry acetone. It dissolves in dry chloroform, quickly separating again apparently with chloroform of crystallization. It gelatinizes under cold water and dissolves on heating, separating again on cooling as a vaseline-like mass. It dissolves with effervescence in conc. sulfuric acid, giving a pale yellow-green, fluorescent solution. The compound also gives the thalleoquinine test.

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[1] *Gazz. chim. ital.*, 13, 530 (1884).

[2] THIS JOURNAL, 39, 1441 (1917)

Subs., 0.1916: 14.35 cc. N (19.0°, 760 mm.).
Subs., 0.1731: 6.92 cc. $AgNO_3$ soln. (1 cc. = 0.001812 g. Cl).
Calc. for $C_{28}H_{32}O_3N_3Cl$: N, 8.51; Cl, 7.18. Found: N, 8.57; Cl, 7.24.

The Hydrochloride.—Quinine chloroacetanilide in absolute alcohol was treated with alcoholic hydrochloric acid, the hydrochloride separating quickly as aggregates of minute, flat needles, and was filtered off after adding an equal volume of dry ether. The crude salt was dissolved in hot absolute alcohol, crystallized by the cautious addition of dry ether, and dried *in vacuo* at room temperature over sulfuric acid and crushed alkali. When rapidly heated to 200°, then slowly, it darkens and melts with decomposition at 204–6° to a deep red mass.

It has a sharp, bitter taste and dissolves readily in water, yielding a solution acid to litmus but not to congo red. It dissolves very readily in methyl alcohol, less easily in absolute alcohol or dry chloroform, and is very difficultly soluble in dry acetone. An aqueous solution gives an amorphous precipitate with excess alkali.

Subs., 0.1881: 13.1 cc. N (24.5°, 758 mm.).
Subs., 0.1258: 9.05 cc. $AgNO_3$ soln. (1 cc. = 0.001812 g. Cl).
Calc. for $C_{28}H_{32}O_3N_3Cl.HCl$: N, 7.93; Cl, 13.37. Found: N, 7.97; Cl, 13.04.

Quinine Chloroacetanilide Nitrate, $C_{20}H_{24}O_2N_2.ClCH_2CONHC_6H_5.HNO_3$.—By analogy with the corresponding derivative of hydroquinine (see below) this salt was originally believed to be quinine acetanilide dinitrate, but as it persistently retained several per cent. of chlorine in spite of attempts to substitute the nitrate ion the preparation was modified as follows: 2 g. of the chloride hydrochloride were dissolved in water with the aid of a drop of dil. nitric acid to drive back dissociation.

A few drops of saturated salt solution were added and then 10% nitric acid until the initial turbidity barely redissolved and crystals began to form. The salt separated rapidly on rubbing and after letting stand in the cold it was filtered off and dissolved in hot water. The solution was then cooled to initial turbidity, cleared with a drop of dil. nitric acid and treated with a few drops of saturated sodium chloride solution, then with 10% nitric acid until crystals began to separate. After finally letting stand in the ice box the deposit of thin, nacreous platelets was filtered off and washed with a little ice water. The yield was 1.4 g. When rapidly heated to 100°, then slowly, the salt decomposes at 201–3° with preliminary browning and softening. It is appreciably soluble in water at room temperature, but is almost insoluble in the presence of nitric acid. It is readily soluble in boiling water, less easily in boiling methyl or ethyl alcohol, and difficultly in boiling acetone or chloroform. The air-dry salt contains no water of crystallization.

Subs. 0.1163: 10.9 cc N (28.5°, 763 mm.)
Subs. 0.1352: 4.54 cc $AgNO_3$ soln (1 cc = 0.001794 g Cl).
Calc for $C_{28}H_{32}O_3N_3Cl.HNO_3$: N, 10.06; Cl, 6.37. Found: N, 10.65; Cl, 6.03.

Quinine *p*-Chloroacetylamino-phenol, $C_{20}H_{24}O_2N_2.ClCH_2CONHC_6H_4$-$OH(p$-$)$.—4.7 g. of *p*-chloroacetylamino-phenol[1] were used. Toward the end a dark tar separated, and on standing overnight a portion of this crystallized. The acetone was poured off and the crude material dissolved in a little warm absolute alcohol and treated with several volumes of dry acetone. Dry, alcohol-free ether was then cautiously added until a slight permanent turbidity had formed, and after treating with boneblack, the filtrate was seeded. On rubbing and stirring and occasionally adding additional small amounts of dry ether, 5.1 g. of the chloride separated as rosets of minute, faintly pinkish needles. The salt was washed with dry acetone, dried *in vacuo* over sulfuric acid to remove adhering solvent, and then air-dried, coming to equilibrium with approximately 1.5 molecules of water of crystallization. It then dissolves with difficulty in cold water, freely on heating, separating on cooling as a jelly. An aqueous solution gives a precipitate with sodium hydroxide. The anhydrous salt softens at about 180–90° to an orange red jelly which is completely fluid at about 205° and slowly evolves gas. It dissolves readily in methyl or ethyl alcohol, forms a gum under dry chloroform, and is sparingly soluble in cold, dry acetone, more easily on warming.

Subs. (air-dry), 0.4644: loss, 0.0258 *in vacuo* at 100° over H_2SO_4.
Calc for $C_{28}H_{32}O_4N_3Cl.1.5H_2O$: H_2O, 5.03. Found: 5.56.
Subs. (anhydrous), 0.1218: 8.6 cc N (24.0°, 759 mm.). Subs., 0.1998: AgCl, 0.0533.
Calc for $C_{28}H_{32}O_4N_3Cl$: N, 8.24; Cl, 6.96. Found: N, 8.11; Cl, 6.60.

Quinine *o*-Chloroacetylamino-benzamide, $C_{20}H_{24}O_2N_2.ClCH_2CONH$-$C_6H_4CONH_2(o$-$)$.—4.25 g. of *o*-chloroacetylamino-benzamide[1] were used, with alcohol as the solvent. This was then boiled off and the gummy residue taken up in dry acetone, the chloride soon crystallizing from the dark brown, fluorescent solution. The yield was 4.7 g. The crude salt was purified by dissolving in hot, dry chloroform, treating with boneblack, filtering, and adding several volumes of dry acetone, then by recrystallization from absolute alcohol, in which it is sparingly soluble in the cold, quite easily on boiling. It forms pale tan rhombs containing 3.5 molecules of water of crystallization or 1.5 molecules of alcohol. When rapidly heated to 175°, then slowly, the anhydrous salt melts at 178–9° with gas evolution to a red-brown liquid. $[\alpha]_D^{28} = -164.4°$ in absolute alcohol, $c = 0.979$. It is soluble in dry chloroform, difficultly so in cold absolute alcohol, readily on boiling with a yellow color, and is almost insoluble in boiling benzene. A solution in dilute acid gives a gummy precipitate with excess sodium hydroxide and if this is washed well with water and rubbed, it gives the microcrystalline, difficultly soluble quaternary base.

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[1] This Journal, 39, 1442 (1917).

Subs. (air-dry), 0.7616: loss, very slow, 0.0789 *in vacuo* at 100° over H_2SO_4

Calc. for $C_{29}H_{33}O_4N_4Cl.3.5H_2O$: H_2O, 10.52. For $1.5C_2H_5OH$, 11.40. Found: 10.36

Subs (anhydrous), 0.1325: 11.9 cc. N (18.0°, 749 mm.). Subs., 0.2289: AgCl, 0.0588

Calc. for $C_{29}H_{33}O_4N_4Cl$: N, 10.44; Cl, 6.61. Found: N, 10.39; Cl, 6.36

(D) Quaternary Salts of Quinidine.

Quinidine Methochloride.—19.9 g. of quinidine methiodide were converted into the methochloride as usual, salting out the product cautiously with sodium chloride solution. Treated in absolute alcoholic solution after filtering from sodium chloride, with several volumes of dry ether the salt crystallizes on rubbing as aggregates of prisms containing solvent equivalent to one molecule of water of crystallization when air dry. The yield was 8.5 g. The anhydrous salt melts with decomposition at 250–1° and gives $[\alpha]_D^{21} = +253.1°$ in water, $c = 1.505$. It dissolves readily in water, methyl or ethyl alcohol, or chloroform and is almost insoluble in dry acetone or benzene.

Subs. (air-dry), 0.5200: loss, 0.0245 *in vacuo* at 100° over H_2SO_4

Calc. for $C_{21}H_{27}O_2N_2Cl.H_2O$: H_2O, 4.59. Found: 4.71

Subs. (anhydrous), 0.2216: AgCl, 0.0837

Calc. for $C_{21}H_{27}O_2N_2Cl$: Cl, 9.46. Found: 9.35

Quinidine Benzyl Chloride.—The components were allowed to stand in a warm place in acetone solution for 15–20 days. After boiling off the acetone the residue soon began to crystallize and the process was hastened by adding dry acetone. The collected salt was ground up with dry acetone, heated to boiling, cooled, filtered again and washed with dry acetone. The yield was 85% of the quinidine used. The chloride forms pale yellow, hair-like needles, containing approximately 2 molecules of water of crystallization when air-dry. The anhydrous salt gradually melts and decomposes up to 180° when heated and gives $[\alpha]_D^{21.5} = +219.9°$ in water, $c = 0.632$. It softens under dry methyl or ethyl alcohol or dry chloroform, dissolving readily, and is more sparingly soluble in dry acetone. The chloride also dissolves readily in water.

Subs. (air-dry), 0.7596: loss, 0.0609 *in vacuo* at 80°, then 100° over H_2SO_4.
Calc. for $C_{27}H_{31}O_2N_2Cl.2H_2O$: H_2O, 7.40. Found: 8.02.
Subs. (anhydrous), 0.1350: 7.5 cc. N (24.0°, 749 mm.).
Subs., 0.1557: 6.70 cc. $AgNO_3$ soln. (1 cc. = 0.001812 g. Cl).
Calc. for $C_{27}H_{31}O_2N_2Cl$: N, 6.22; Cl, 7.87. Found: N, 6.29; Cl, 7.80.

Quinidine Iodoacetamide.—The quaternary salt crystallized in practically quantitative yield on suspending quinidine in hot acetone, adding one equivalent of iodoacetamide, shaking until clear, and letting stand overnight. As so obtained the salt forms a paste under water, crystallizing on rubbing. Recrystallized from water it forms rosets of long, narrow plates containing 1.5 molecules of water of crystallization. The anhydrous iodide melts to a yellow jelly at 165–70°, gradually liquefying and darkening until entirely fluid and filled with bubbles at about 190°. $[\alpha]_D^{22.5} = +166.2°$ in absolute alcohol, $c = 1.008$. It becomes pasty under methyl or ethyl alcohol, dissolving readily, and also dissolves in chloroform. The hydrate is easily soluble in hot water, sparingly in the cold, and dissolves readily in acetone, separating immediately on rubbing, presumably as a less hydrated form.

Subs. (air-dry), 0.6898: loss, 0.0330 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{22}H_{28}O_3N_3I.1.5H_2O$: H_2O, 5.04. Found: 4.78.
Subs. (anhydrous), 0.2585: AgI, 0.1180.
Calc. for $C_{22}H_{28}O_3N_3I$: I, 24.93. Found: 24.67.

Quinidine Chloroacetamide.—After recrystallization from water this salt formed rosets of prismatic needles containing one molecule of water of crystallization, the yield being about 50% of the quaternary iodide used. The anhydrous salt melts at 187–91° to a yellow jelly, gradually darkening and finally liquefying with decomposition at about 205°. $[\alpha]_D^{22} = +207.2°$ in water, $c = 1.031$. The chloride is soluble in cold water or alcohol, more readily in methyl alcohol, and very sparingly in chloroform or acetone.

Subs. (air-dry), 0.6128: loss, 0.0280 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{22}H_{28}O_3N_3Cl.H_2O$: H_2O, 4.14. Found: 4.57.
Subs. (anhydrous), 0.1300: 11.2 cc. N (21.5°, 759 mm.).
Subs., 0.2566: AgCl, 0.0861.
Calc. for $C_{22}H_{28}O_3N_3Cl$: N, 10.06; Cl, 8.49. Found: N, 9.98; Cl, 8.30.

Quinidine Iodoacetylurea.—Equimolecular amounts of quinidine and iodoacetylurea[1] were boiled in acetone until clear. The next day most of the solvent was boiled off and the residue taken up in hot water, treated with boneblack, filtered, and allowed to cool. The iodide separates in almost quantitative yield on rubbing. Recrystallized again from water it forms rosets of minute plates containing 3 molecules of water of crystallization. When rapidly heated to 165°, then slowly, the anhydrous salt melts at 170–5° to an orange mass which slowly evolves gas and blackens. It is difficultly soluble in cold water, readily in hot, and dissolves easily at room temperature in methyl or ethyl alcohol or acetone. It dissolves slowly in dry chloroform and only sparingly in benzene.

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[1] **Iodoacetylurea,** $ICH_2CONHCONH_2$.—13.6 g. of finely powdered chloroacetylurea were added to a solution of 15 g. of dry sodium iodide in 100 cc. of dry acetone, shaken for 2.5 hours, and let stand overnight (cf. L. Finkelstein, *Ber.*, 43, 1528 (1910)). The mixture, now a paste of minute crystals of the iodo compound, was diluted with water and filtered. The crude iodoacetylurea was recrystallized from 50% alcohol, in which it is quite sparingly soluble, even at the boiling point. 15.4 g. separated as flat prisms which melt and decompose at 182–4° with preliminary darkening and partial de-

Subs. (air-dry), 0.6290: loss, 0.0532 *in vacuo* at 100° over H_2SO_4

Calc for $C_{23}H_{29}O_4N_4I.3H_2O$. H_2O, 8 91. Found: 8 46.

Subs. (anhydrous), 0 1360 12 6 cc N (30.0°, 755 mm). Subs., 0 1658. AgI, 0.0681.

Calc. for $C_{23}H_{29}O_4N_4I$: N, 10 14; I, 22.98. Found N, 10.37; I, 22 20.

Quinidine Chloroacetylurea.—The chloride, prepared from the iodide with silver chloride, was recrystallized from a small volume of water, forming rosets of spears containing 3.5 molecules of water of crystallization. The anhydrous salt melts and swells at 176–8°, with darkening, and gives $[\alpha]_D^{26.5} = +170.9°$ in water, $c = 1.325$. It dissolves readily in water or methyl or ethyl alcohol, less easily in dry acetone or chloroform, and difficultly in benzene. The hydrate dissolves rather sparingly in cold water, readily on heating and yields a highly supersaturated solution on cooling. Such a solution gives an oily precipitate on adding excess sodium hydroxide and evolves ammonia on boiling.

Subs. (air dry), 0 8849. loss, 0.1041 *in vacuo* at 80° over H_2SO_4.

Calc. for $C_{23}H_{29}O_4N_4Cl.3.5H_2O$ H_2O, 12.03. Found: 11.77.

Subs. (anhydrous), 0.1418: 15 3 cc. N (28 0°, 762 mm.). Subs., 0.1457: 6.07 cc. $AgNO_3$ soln. (1 cc. = 0.001812 g. Cl).

Calc. for $C_{23}H_{29}O_4N_4Cl$. N, 12.17; Cl, 7.70. Found. N, 12.27; Cl, 7.55.

(E) Quaternary Salts of Hydroquinine.

Hydroquinine Methiodide.—Equimolecular quantities of the base[1] and methyl iodide in chloroform gave the salt in a yield of 78% of the theoretical amount, separation being completed with about two volumes of acetone. Recrystallized from absolute alcohol the methiodide forms faintly yellow prisms which are anhydrous when air-dry. It melts partially at about 170° and liquefies completely, with decomposition at 233–5°. $[\alpha]_D^{20.5}$ is —107.6° in absolute alcohol, $c = 0.855$. The salt is somewhat soluble in cold water, more easily in alcohol, and

composition. The iodo compound dissolves rather difficultly in boiling water or boiling acetone and very sparingly in chloroform. It is quite soluble in cold methyl alcohol, less readily in the cold in ethyl alcohol, but more freely on boiling. It dissolves in dilute alkali and does not seem to be as active an irritant as chloroacetylurea.

Subs., 0.1510: (Kjeldahl) 18.6 cc. 0.0714 *N* HCl.

Calc. for $C_3H_5O_2N_2I$: N, 12.29. Found: 12.32.

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[1] Ger. pat. 252136; THIS JOURNAL, 41, 819 (1919).

readily in methyl alcohol or chloroform. Hesse[1] states that the methiodide crystallizes with one molecule of alcohol of crystallization and melts at 218° when dried.

Subs, 0 2086. AgI, 0 1048
Calc for $C_{21}H_{29}O_2N_2I$ I, 27 10 Found. 27.15.

Hydroquinine Methochloride.—The salt crystallizes from water as balls of hair-like needles containing 2 molecules of water of crystallization, as stated by Hesse. When rapidly heated to 155°, then slowly, the anhydrous methochloride forms a paste at 157–9°, and on further heating finally becomes a yellow liquid filled with bubbles at 172–3°. Hesse gives the melting point as 168°. $[\alpha]_D^{21.5}$ in water is —162.9°, $c = 1.470$. The anhydrous salt also dissolves very easily in methyl or ethyl alcohol, less readily in dry acetone.

Subs (anhydrous), 0 2760 AgCl, 0 1052
Calc for $C_{21}H_{29}O_2N_2Cl$ Cl, 9 41 Found 9 43

Hydroquinine Benzyl Chloride.—The components were boiled for about 15 hours in dry acetone. After long standing the acetone was boiled off and the dark residue taken up in dry methyl alcohol. The chloride crystallized rapidly on adding several volumes of dry ether and was recrystallized from water, separating slowly on seeding at room temperature as a crust of rhombs and prisms containing one molecule of water of crystallization. An additional quantity of equal purity was obtained by adding saturated sodium chloride solution to the aqueous mother liquor, letting stand, and washing the crystals with cold water. The total yield was 3 g., starting with 3.6 g. of the base. When rapidly heated to 200°, then slowly, the anhydrous chloride melts at 202–3.5° to a dark red, viscous liquid which soon decomposes. $[\alpha]_D^{23}$ in water is —196.9°, $c = 0.787$. It dissolves readily in methyl or ethyl alcohol or chloroform, less easily in dry acetone, and melts under hot benzene, dissolving with difficulty. The air-dry salt dissolves rather sparingly in cold water, quite readily on boiling, the solution having a weak, bitter taste. A not too dilute aqueous solution gives immediate precipitates of the nitrate and permanganate with the appropriate salts. Solutions in dil. sulfuric or nitric acid have a marked blue fluorescence, while the solution in dil. hydrochloric acid is pale yellow and does not fluoresce.

Subs (air-dry), 0 7928 loss, 0 0281 *in vacuo* at 100° over H_2SO_4 Subs, 0 1238. 7 10 cc. N (25 5°, 755 mm) Subs, 0 1520 (Kjeldahl, with H_2SO_4, K_2SO_4, and crystal of $CuSO_4$) 8 8 cc. 0.0714 *N* HCl Subs, 0 1203· 5 1 cc $AgNO_3$ soln (1 cc. = 0 001794 g Cl).

Calc. for $C_{27}H_{33}O_2N_2Cl\ H_2O$· H_2O, 3.83; N, 5.95, Cl, 7 53. Found. H_2O, 3.54; N, 6.51, 5 79; Cl, 7.61.

Hydroquinine Iodoacetamide.—Acetone was used as solvent and after several hours it was boiled off and hot water added, the iodide crystallizing on cooling and rubbing as prismatic plates. The yield was almost quantitative. Recrystallized from water the salt forms prismatic needles containing between 2.5 and 3 molecules of water of crystallization. The anhydrous salt gradually softens to a yellow jelly above 145°, deepening in color as the temperature is raised, and becoming entirely fluid at about 185°. $[\alpha]_D^{23.5}$ in absolute alcohol is $-121.5°$, $c = 0.976$. The dried salt also softens and dissolves readily in dry methyl or ethyl alcohol, dry acetone, or dry chloroform.

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[1] *Ann* 241, 275 (1887).

Subs (air-dry), 0 6120 loss, 0 0534 *in vacuo* at 100° over H_2SO_4
Calc for $C_{22}H_{30}O_3N_3I\ 2\ 5H_2O \cdot H_2O$, 8 10 Found 8 72
Subs. (anhydrous), 0 2039 AgI, 0 0933
Calc for $C_{22}H_{30}O_3N_3I$ I, 24 83 Found· 24 72

Hydroquinine Chloroacetamide.—Instead of adding sodium chloride to the filtrate from the silver iodide precipitate the solution was allowed to stand overnight, filtered from a small amount of a substance crystallizing in silky needles, and the filtrate concentrated to dryness *in vacuo*. The residue was taken up in absolute alcohol, concentrated to dryness *in vacuo*, again taken up in absolute alcohol, filtered from a slight turbidity with the aid of boneblack, and concentrated as before, giving a friable, white, amorphous residue which could easily be removed from the flask. The dried salt turns yellow and softens at about 160–75° to a jelly which gradually darkens and liquefies completely with gas evolution at about 195°. $[\alpha]_D^{23} = -129.1°$ in water, $c = 0.852$. The product is very easily soluble in acetone or chloroform and also dissolves readily in cold water.

Subs (anhydrous), 0 1356 12 2 cc N (27 5°, 758 mm)
Subs., 0 1451 6 92 cc $AgNO_3$ soln (1 cc = 0 001812 g. Cl)
Calc for $C_{22}H_{30}O_3N_3Cl$ N, 10 02, Cl, 8 45 Found N, 10 19, Cl, 8 64

Hydroquinine Chloroacet-methylamide, $C_{20}H_{26}O_2N_2.ClCH_2CONHCH_3$.—This salt was obtained directly from chloroacet-methylamide[1] in boiling dry acetone. As the product could neither be crystallized nor converted into a crystalline bromide or hydrochloride it was precipitated with dry ether, dried *in vacuo* at room temperature over sulfuric acid, and pulverized. The salt intumesces at 110–20°, gradually melting above this to a glassy mass by the time 160° is reached, and forming a dark brown liquid at about 200°. It dissolves readily in methyl or ethyl alcohol, acetone, chloroform, benzene, or water.

Subs., 0.1340. 10 4 cc N (18.0°, 764 mm)
Subs, 0.1165 5.09 cc $AgNO_3$ soln (1 cc = 0 001794 g Cl)
Calc. for $C_{23}H_{32}O_3N_3Cl$. N, 9 69, Cl, 8 17 Found· N, 9 16, Cl, 7 84

Hydroquinine Chloroacet-ethylamide.—This salt was prepared in the same way, using chloroacet-ethylamide.[2] On adding dry ether the gummy material crystallized partially, but as the crystals softened to a gum on desiccation or air-drying, and as an attempt at recrystallization by dissolving in dry acetone and precipitating with dry ether proved no better, the substance was left in the crude state and dried *in vacuo* over sulfuric acid. It melted to a yellowish jelly at 110–35°, becoming completely fluid at about 160°. In solubility it resembles the methyl compound.

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[1] This Journal, 41, 472 (1919).

[2] *J. Biol. Chem.*, 21, 140 (1915).

Subs., 0.1680: 13.7 cc. N (23.0°, 751 mm.). Subs., 0.1561: AgCl, 0.0479.
Calc. for $C_{24}H_{34}O_3N_3Cl$: N, 9.39; Cl, 7.92 Found: N, 9.30; C, 7.59.

Hydroquinine Chloroacet-dimethylamide, $C_{20}H_{28}O_2N_2.ClCH_2CON(CH_3)_2$.—An amorphous salt was obtained from chloroacet-dimethylamide,[1] melting partially and intumescing at 130–40°, becoming transparent at about 180°, and liquefying completely at about 200°. It resembles the monomethyl and -ethyl derivatives in its solubility relationships.

Subs., 0.1362: 10.4 cc. N (19.5°, 765 mm.).
Subs., 0.1797: 7.68 cc. $AgNO_3$ soln. (1 cc. = 0.001794 g. Cl).
Calc. for $C_{24}H_{34}O_3N_3Cl$: N, 9.39; Cl, 7.92. Found: N, 8.97; Cl, 7.67.

Hydroquinine Chloroacet-diethylamide, $C_{20}H_{28}O_2N_2.ClCH_2CON(C_2H_5)_2$.—1.6 g. of chloroacet-diethylamide[2] were used. On adding ligroin until the initial turbidity just redissolved the chloride crystallized on standing as rosets of prismatic needles, precipitation being completed by the addition of more ligroin and letting stand. The yield was 3.5 g. On dissolving in not too little dry chloroform and treating cautiously with ligroin, seeding, and adding more ligroin from time to time the salt forms minute prisms containing solvent approximately equivalent to one molecule of water of crystallization. The anhydrous salt darkens somewhat above 205° and melts and decomposes at 209–10°. $[\alpha]_D^{27.5} = -84.8°$ in water, $c = 0.854$. It dissolves readily at room temperature in water, methyl or ethyl alcohol, or chloroform, sparingly in cold acetone, more easily on heating, and is almost insoluble in benzene. It has a sharp, bitter taste.

Subs. (air-dry), 0.6028: loss, 0.0182 *in vacuo* at 80° over H_2SO_4.
Calc. for $C_{26}H_{38}O_3N_3Cl.H_2O$: H_2O, 3.65. Found: 3.02.
Subs. (anhydrous), 0.1226: 10.0 cc. N (30.0°, 757 mm.). Subs., 0.1247: 5.15 cc. $AgNO_3$ soln. (1 cc. = 0.00181 g. Cl).
Calc. for $C_{26}H_{38}O_3N_3Cl$: N, 8.84; Cl, 7.45. Found: N, 9.16; Cl, 7.48.

Hydroquinine Chloroacetyl-benzylamine, $C_{20}H_{26}O_2N_2.ClCH_2CONHCH_2C_6H_5$.—Starting with chloroacetyl-benzylamine[3] in dry acetone the salt crystallized from the reaction mixture. Recrystallized from butyl alcohol[4] the chloride separates as delicate, glistening needles. The anhydrous salt melts at 197–8° to an orange liquid containing bubbles. $[\alpha]_D^{23}$ in water is $-42.5°$, $c = 0.670$. The compound dissolves fairly readily in water, easily in methyl or ethyl alcohol, or chloroform. A dilute aqueous solution gives a precipitate with sodium hydroxide.

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[1] *J. Biol. Chem.*, 21, 148 (1915).

[2] *Ibid.*, 21, 149 (1915).

[3] *Ibid.*, 20, 686 (1915).

[4] We have found commercial butyl alcohol to be a very useful solvent.

Subs., 0.1409: 10.2 cc. N (23.0°, 744 mm.) Subs., 0.1697: 6.45 cc. $AgNO_3$ soln. (1 cc. = 0.00181 g. Cl).

Calc. for $C_{29}H_{34}O_3N_3Cl$: N, 8.29; Cl, 6.99. Found: N, 8.18; Cl, 6.88.

Hydroquinine Chloroacetanilide.—On adding hot water to the residue after boiling off the acetone the crude product separated at first oily on cooling but soon crystallized in almost quantitative yield. Recrystallized from 50% alcohol the chloride forms rosets of delicate needles containing 3 molecules of water of crystallization. When anhydrous it softens to an orange jelly at 160–70°, liquefying completely at about 210° with darkening and slow gas evolution. $[\alpha]_D^{24} = -95.9°$ in absolute alcohol, $c = 0.824$. It dissolves readily in methyl or ethyl alcohol, acetone, chloroform, or benzene, and only sparingly in dry ether. The hydrate is difficultly soluble in cold water, more readily on heating, and is rather sparingly soluble in cold 50% alcohol. It dissolves in 10% aqueous hydrochloric acid, the *hydrochloride* soon separating as sheaves of minute needles.

Subs. (air dry), 0.5450: loss, 0.0534 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{28}H_{34}O_3N_3Cl.3H_2O$: H_2O, 9.83. Found: 9.80.

Subs. (anhydrous), 0.1469: 11.0 cc. N (26.0°, 762 mm.). Subs., 0.1556: AgCl, 0.0443.

Calc. for $C_{28}H_{34}O_3N_3Cl$: N, 8.48; Cl, 7.15. Found: N, 8.58; Cl, 7.05.

Hydroquinine Acetanilide Dinitrate, $C_{20}H_{26}O_2N_2.O_3NCH_2CONHC_6H_5.HNO_3$.—One g. of hydroquinine chloroacetanilide was dissolved in about 100 cc. of boiling water, and a few drops of dil. nitric acid added on cooling. The solution was chilled, acidified strongly with dil. nitric acid and rubbed, 0.6 g. of the dinitrate separating as long, delicate needles. The salt was washed with a little ice-cold water and air-dried, containing then approximately 2 molecules of water of crystallization. When heated the anhydrous salt melts to a jelly at about 145–50° with slight preliminary softening, then darkens and intumesces. It softens under the usual anhydrous solvents, dissolving readily in dry methyl or ethyl alcohol or dry acetone, sparingly in dry chloroform, even on boiling, and is practically insoluble in boiling benzene. The hydrate dissolves very sparingly in cold water, fairly readily on boiling, with a faint greenish yellow color.

Subs. (air-dry), 0.5877: loss, 0.0317 *in vacuo* at room temp. over H_2SO_4 + NaOH.

Calc. for $C_{28}H_{34}O_3N_3.NO_3.HNO_3.2H_2O$: H_2O, 5.80. Found: 5.39.

Subs. (anhydrous), 0.1265: 13.4 cc. N (23.0°, 755 mm.).

Calc. for $C_{28}H_{34}O_3N_3.NO_3.HNO_3$: N, 11.97. Found: 12.14.

Hydroquinine *m*-Nitro-chloroacetanilide.—The gelatinous reaction mixture was disintegrated with hot water and let stand. The resulting precipitate, recrystallized first from 25%, then from 50% alcohol, separated as pale drab-colored, minute needles which contained approximately 2 molecules of water of crystallization. When slowly heated, the anhydrous salt begins to soften at 150°, gradually melting to a brownish jelly up to 160°, and liquefying completely and decomposing at 195–200°. It softens under and dissolves readily with a pale yellow color in dry methyl or ethyl alcohol, dry acetone, dry chloroform, or ethyl acetate, dissolving sparingly in cold benzene and readily on boiling. The hydrate is quite difficultly soluble in cold water, more easily on boiling. An aqueous suspension turns bright yellow and flocculates with a few drops of aqueous sodium hydroxide.

Subs. (air-dry), 0 5443: loss, 0 0374 *in vacuo* at 100° over H_2SO_4

Calc for $C_{28}H_{33}O_5N_4Cl\ 2H_2O$ H_2O, 6 25 Found 6 87

Subs. (anhydrous), 0.1279. 12 0 cc. N (24 0°, 759 mm.) Subs , 0 1175: 4.05 cc $AgNO_3$ soln. (1 cc = 0 001794 g Cl)

Calc. for $C_{28}H_{33}O_5N_4Cl$: N, 10 36; Cl, 6 56. Found· N, 10 77; Cl, 6 19.

Hydroquinine *m*-Chloroacetylamino-acetanilide, $C_{20}H_{26}O_2N_2.ClCH_2CONHC_6H_4NHCOCH_3$(*m*-).—Starting with *m*-chloroacetylamino-acetanilide,[1] a gummy quaternary salt separated, from which the acetone was eventually poured off and the residue boiled with dry methyl ethyl ketone. The gum which separated on cooling was filtered off and on letting stand and rubbing the chloride separated from the filtrate as practically colorless, radiating masses of minute crystals. A further quantity was obtained by again extracting the crude gummy material with the filtrate. The air-dry salt contained solvent of crystallization corresponding to 3 to 3.5 molecules of water. When heated the anhydrous salt gradually melts to an orange mass above 150°, with slow gas evolution, becoming completely fluid at about 205–10°. It first softens under, and then dissolves freely in dry methyl or ethyl alcohol, also dissolves readily in chloroform, and is very difficultly soluble in boiling dry acetone, benzene, or ethyl acetate.

Subs (air-dry), 0 4457 loss, 0 0432 *in vacuo* at 80° over H_2SO_4

Calc. for $C_{30}H_{37}O_4N_4Cl\ 3H_2O$ H_2O, 8 91 Found: 9.69.

Subs. (anhydrous), 0 1309: 11 25 cc. N (21.5°, 755 mm) Subs., 0 1412: 4.92 cc. $AgNO_3$ soln. (1 cc = 0 001794 g Cl)

Calc. for $C_{30}H_{37}O_4N_4Cl$: N, 10.13; Cl, 6 41. Found: N, 9 90, Cl, 6.25.

Hydroquinine *p*-Chloroacetylamino-acetanilide.—In the case of the sparingly soluble *p*-chloroacetylamino-acetanilide[2] absolute alcohol was used as solvent. After letting stand in the cold the insoluble material was filtered off, and the filtrate concentrated to small bulk. The residue was taken up in boiling water, treated with boneblack and the filtrate cooled, diluting so that it became only faintly turbid at room temperature. After filtering again the solution was seeded with crystals obtained by adding sodium chloride to a test portion. The crude quaternary salt was recrystallized from water, separating as rosets and sheaves of delicate, silky needles. Additional amounts were obtained by adding sodium chloride to the mother liquors. The air-dry salt contains 3 molecules of water of crystallization and dissolves sparingly in cold water, more easily on heating. The anhydrous chloride begins to soften at about 160° and darkens and becomes completely fluid, with slow gas evolution, at about 205°. It dissolves readily in methyl or ethyl alcohol, acetone, or chloroform, and only sparingly in boiling benzene or ethyl acetate. Analysis indicated that the substance was not entirely pure.

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[1] THIS JOURNAL, 39, 1448 (1917).

[2] *Ibid.*, 39, 1455 (1917).

Subs (air-dry), 0.5336: loss, 0.0477 *in vacuo* at room temp over H_2SO_4

Calc for $C_{30}H_{37}O_4N_4Cl.3H_2O$ H_2O, 8.91 Found 8.94

Subs. (anhydrous), 0.1403 12.0 cc N (22.0°, 751 mm) Subs, 0.1260 4.0 cc $AgNO_3$ soln (1 cc = 0.001794 g Cl)

Calc for $C_{30}H_{37}O_4N_4Cl$ N 10.13; Cl, 6.41 Found. N, 9.79; Cl, 5.70

Hydroquinine *p*-Chloroacetylamino-dimethylaniline, $C_{20}H_{26}O_2N_2.Cl\text{-}CH_2CONHC_6H_4N(CH_3)_2(p\text{-})$.—After boiling off the acetone the residue, using 3.5 g. of base, was taken up in about 500 cc. of boiling water and treated with boneblack, yielding 4.3 g. of the crystalline salt on cooling. Recrystallized from 50% alcohol it separates as aggregates of minute, cream-colored needles containing 2.5 molecules of water of crystallization and dissolving very difficultly in cold water, quite easily on boiling. An aqueous suspension gives a brownish rose color with ferric chloride. The anhydrous salt gradually melts to a jelly at about 165°, becoming completely fluid, with partial decomposition at about 200°. $[\alpha]_D^{18.5}$ = −82.9° in absolute alcohol, c = 1.037. It softens under and dissolves freely in dry methyl or ethyl alcohol, dry acetone, or dry chloroform.

Subs. (air-dry), 0.5172: loss, 0.0407 *in vacuo* first at room temp, then 80° over H_2SO_4.

Calc. for $C_{30}H_{39}O_3N_4Cl.25H_2O$ H_2O, 7.72 Found. 7.87

Subs (anhydrous), 0.1185: 10.4 cc N (20.5°, 763 mm) Subs, 0.1196: 4.2 cc. $AgNO_3$ soln (1 cc = 0.001794 g. Cl)

Calc for $C_{30}H_{39}O_3N_4Cl$ N, 10.39, Cl, 6.58 Found: N, 10.25; Cl, 6.30

Hydroquinine *p*-Chloroacetylamino-diethylaniline.—In the case of *p*-chloroacetylamino-diethylaniline[1] the reaction mixture was diluted with dry acetone and the salt precipitated as amorphous flocks with the aid of dry ether. The product was filtered off, washed with a little dry ether, dried, and then dissolved in hot ethyl acetate and seeded while still warm with a few of the crystals left in the reaction flask on evaporation of the solvent. On letting stand in a warm place the salt separated slowly as sheaves of delicate needles. The air dry product still possessed the odor of ethyl acetate. The anhydrous salt begins to soften at about 150°, and when slowly heated above this point forms a transparent jelly at 165–70°, and a red fluid at 190–5°, with slight gas evolution. $[\alpha]_D^{20}$ =

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[1] *J. Biol. Chem.*, **21**, 115 (1915).

—80.5° in absolute alcohol, c = 1.118. It dissolves readily in methyl or ethyl alcohol, acetone, chloroform, or benzene, and also in boiling ethyl acetate, although sparingly in the cold. It is very difficultly soluble in cold water, more easily on boiling. An aqueous suspension gives a slowly-developing salmon color with ferric chloride.

Subs (anhydrous), 0 1277: 11 0 cc N (20 5°, 757 mm) Subs, 0 1034: 3.64 cc. $AgNO_3$ soln (1 cc = 0.001794 g Cl).

Calc for $C_{28}H_{43}O_3N_4Cl$: N, 9 89, Cl, 6 26 Found N, 9 99, Cl, 6 32.

Hydroquinine *o*-Chloroacetylamino-phenol.—To the reaction mixture from *o*-chloroacetylamino-phenol,[1] a few cc. of absolute alcohol were added and then dry ether and ligroin to incipient turbidity. The quaternary salt crystallized on rubbing and letting stand. Recrystallized by dissolving in hot absolute alcohol and adding dry ether until just turbid, it separated on seeding as rosets of long, flat platelets containing solvent equivalent to 1.5 molecules of water of crystallization. It dissolves sparingly in cold water, more freely on heating, separating as a jelly on cooling. The anhydrous salt gradually melts to a jelly above 155°, finally reddens, and becomes completely fluid and evolves gas at 185°. It dissolves very easily in dry methyl alcohol and less readily in absolute alcohol or dry acetone. An alkaline suspension couples with diazotized sulfanilic acid.

Subs. (air-dry), 0 5750 loss, 0 0308 *in vacuo* at 100° over H_2SO_4

Calc. for $C_{28}H_{34}O_4N_3Cl$ 1 $5H_2O$ H_2O, 5 01 Found 5 36

Subs (anhydrous), 0 1449 10 35 cc N (20 5°, 758 mm) Subs, 0 1539 AgCl, 0.0469

Calc for $C_{28}H_{34}O_4N_3Cl$ N, 8.21, Cl, 6 93 Found N, 8 29, Cl, 7 54

Hydroquinine *m*-Chloroacetylamino-phenol.—Starting with 1.9 g. of *m*-chloroacetylamino-phenol[2] 4 5 g. of the salt crystallized from the reaction mixture as hard nodules. Recrystallized from not too little 50% alcohol, seeding and rubbing while still warm, the chloride separates as cream-colored aggregates of microscopic leaflets containing 3 molecules of water of crystallization. If care is not taken the solution gelatinizes. The anhydrous salt softens and sinters above 160°, melts to a reddish jelly at about 180–5°, and is completely fluid, with slow gas evolution, at about 205°. $[\alpha]^{21}_{D}$ = —115.7° in absolute alcohol, c = 0.800. It first softens under, then resolidifies, dissolving freely, in absolute alcohol or dry methyl alcohol, also softening under boiling dry acetone and dissolving with difficulty. The salt is very difficultly soluble in cold water, more easily on boiling, and is readily soluble in hot 50% alcohol, quite sparingly in the cold.

Subs. (air-dry), 0.5070: loss, 0 0489 *in vacuo* at 80° over H_2SO_4.

Calc. for $C_{28}H_{34}O_4N_3Cl$ $3H_2O$ H_2O, 9 56 Found: 9.64.

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[1] THIS JOURNAL, 41, 458 (1919).

[2] *Ibid.*, 39, 1442 (1917)

Subs. (anhydrous), 0.1262: 9.55 cc N (26.0°, 754 mm.). Subs., 0.1535: AgCl, 0.0409.

Calc. for $C_{28}H_{34}O_4N_3Cl$. N, 8.21; Cl, 6.93 Found. N, 8.57; Cl, 6.59.

The Hydrochloride.—The purified salt was rubbed in a mortar with 1 : 1 hydrochloric acid, yielding a pasty mass which eventually crystallized. Recrystallized from hot water containing a little hydrochloric acid it separates on cooling and seeding as cream-colored prismatic needles and short rods, separation being completed by further small additions of 10 % hydrochloric acid. The hydrochloride contains 4.5 molecules of water of crystallization and dissolves fairly readily in water The anhydrous salt is a pale sulfur-yellow and forms an orange jelly at 195–7°, melting and evolving gas at about 200°. It dissolves readily in methyl or ethyl alcohol and is practically insoluble in dry acetone. It does not dissolve in excess dil. alkali, the suspension coupling with diazotized sulfanilic acid.

Subs (air-dry), 0.5030 loss, 0.0650

Calc. for $C_{28}H_{34}O_4N_3Cl.HCl.4.5H_2O$ H_2O 12.88 Found: 12.92

Subs (anhydrous), 0.1654 AgCl, 0.0860

Calc. for $C_{28}H_{34}O_4N_3Cl.HCl$ Cl, 12.93 Found 12.86.

Hydroquinine *p*-Chloroacetylamino-phenol Hydrochloride.—In the case of *p*-chloroacetylamino-phenol[1] a portion of the quaternary addition product separated as a gum, followed on standing by radiating masses of fibrous needles and the ultimate crystallization of the gum. As the salt could not be recrystallized it was converted into the hydrochloride by dissolving in a slight excess of very dilute hydrochloric acid, adding the conc. acid, with cooling, until slightly turbid, treating with boneblack, and again adding conc. hydrochloric acid to the filtrate until the initial turbidity just redissolved The hydrochloride separated on seeding with crystals obtained from a test portion, precipitation being completed by the further careful addition of conc. hydrochloric acid. Recrystallized from warm water, adding conc. hydrochloric acid to the cooled solution until just turbid, the hydrochloride crystallized as cream-colored rosets of prismatic needles containing 4.5 molecules of water of crystallization, completing the separation as before. The yield was 7.2 g. The salt dissolves fairly readily in water at room temperature and is readily salted out by the addition of hydrochloric acid. An aqueous solution gives a dull, grayish color with ferric chloride. The anhydrous salt is darker than the hydrate and when rapidly heated to 195° then slowly, melts at 196–7° to a red-brown jelly which soon evolves gas. It turns gummy under dry methyl or ethyl alcohol, dissolving readily, and also softens under dry chloroform but remains insoluble. It is also practically insoluble in dry acetone.

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[1] *Loc. cit.*

Subs. (air-dry), 0.4937: loss, 0.0632.

Calc. for $C_{28}H_{34}O_4N_3Cl.HCl.4.5H_2O$: H_2O, 12.88. Found: 12.80.

Subs. (anhydrous), 0.1414: 9.4 cc. N (24.5°, 759 mm.). Subs., 0.1744: AgCl, 0.0907.

Calc. for $C_{28}H_{34}O_4N_3Cl.HCl$: N, 7.67; Cl, 12.93. Found: N, 7.62; Cl, 12.86.

Hydroquinine 4-Chloroacetylamino-pyrocatechol Hydrochloride, $C_{20}H_{26}O_2N_2.ClCH_2CONHC_6H_3(OH)_2.HCl(3,4\text{-})$.—After pouring off the acetone from the gummy precipitate in the case of 4-chloroacetylamino-pyrocatechol[1] 10% aqueous hydrochloric acid was added, as well as a little alcohol to facilitate solution. On cautiously adding further portions of hydrochloric acid and treating with boneblack to remove the first gummy precipitates a clear, red-brown solution was finally obtained. This was seeded with crystals obtained by rubbing a portion of the crude gummy salt with 1 : 1 hydrochloric acid and letting stand. The hydrochloride separated in poor yield as pale yellow needles containing 4.5 molecules of water of crystallization, precipitation being completed by finally adding more acid. The salt dissolves in water, the solution giving an olive-green color with ferric chloride, changing rapidly to yellow-brown. An aqueous solution gave a precipitate with sodium hydroxide, insoluble in excess. When rapidly heated to 195°, then slowly, the anhydrous hydrochloride melts to a jelly at 196–8°, gradually decomposing as the temperature is further raised. It dissolves readily in methyl alcohol, more slowly in absolute alcohol, and is practically insoluble in dry acetone or dry chloroform.

Subs. (air-dry), 0.4249: loss, 0.0530.

Calc. for $C_{28}H_{34}O_5N_3Cl.HCl.4.5H_2O$: H_2O, 12.57. Found: 12.48.

Subs. (anhydrous), 0.1176: 7.4 cc. N (21.5°, 767 mm.). Subs., 0.1758: AgCl, 0.0877.

Calc. for $C_{28}H_{34}O_5N_3Cl.HCl$: N, 7.45; Cl, 12.57. Found: N, 7.36; Cl, 12.34.

Hydroquinine Chloroacetyl-*o*-anisidine.—Starting with 4 g. of chloroacetyl-*o*-anisidine,[2] 7 g. of the crude quaternary salt were finally deposited from the ice-cold solution on seeding with crystals obtained by spontaneous evaporation. The substance was recrystallized from butyl alcohol, letting stand in the ice box, and seeding, 6.4 g. separating as radiating, hair-like needles. The anhydrous compound gradually sinters and softens to a jelly above 110°, turns yellow above 150°, and is completely fluid at about 185°. $[\alpha]_D^{32} = -72.5°$ in absolute alcohol, $c = 0.904$. It softens under and dissolves readily in dry methyl or ethyl alcohol, dry chloroform, or dry acetone, dissolves less readily in benzene, and gives a pale yellow color in conc. sulfuric acid. The air-dry salt dissolves slowly but freely in water.

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[1] THIS JOURNAL, **41**, 468 (1919).

[2] *Ibid.*, **41**, 1451 (1919).

Subs. (anhydrous), 0.1268: 9.2 cc. N (29.5°, 755 mm.). Subs., 0.1337: 5.07 cc. $AgNO_3$ soln. (1 cc. = 0.00181 g. Cl).

Calc. for $C_{29}H_{36}O_4N_3Cl$: N, 7.99; Cl, 6.75. Found: N, 8.14; Cl, 6.87.

Hydroquinine Chloroacetyl-*m*-anisidine.—(From 2 g. of chloroacetyl-*m*-anisidine.[1]) The solvent was boiled off and the residue taken up in 50% alcohol and cautiously diluted with hot water, filtering off the slight turbidity which first formed. On seeding the solution with crystals obtained by several days' standing of a dilute solution of the crude material in hot water, the salt gradually crystallized, especially on the further addition of small quantities of water and occasional warming. Recrystallized by dissolving in alcohol, diluting with ether, and seeding, the quaternary salt separates as radiating aggregates of delicate needles containing solvent equivalent to 3 molecules of water of crystallization when air-dry. The anhydrous salt gradually sinters and softens above 140° and forms an orange fluid at about 190°. $[\alpha]_D^{23} = -102.9°$ in absolute alcohol, $c = 1.292$. It melts under and dissolves readily in the following dry solvents: methyl or ethyl alcohol, chloroform, acetone, or benzene; and dissolves partly in cold water, the solution foaming readily and soon setting to a jelly. It is readily soluble in boiling water.

Subs. (air-dry), 0.7289: loss, 0.0715 *in vacuo* at 80° over H_2SO_4.

Calc. for $C_{29}H_{36}O_4N_3Cl.3H_2O$: H_2O, 9.32. Found: 9.81.

Subs. (anhydrous), 0.1489: 10.5 cc. N (25.5°, 760 mm.). Subs., 0.1085: 3.9 cc. $AgNO_3$ soln. (1 cc. = 0.001794 g. Cl).

Calc. for $C_{29}H_{36}O_4N_3Cl$: N, 7.99; Cl, 6.75. Found: N, 8.07; Cl, 6.45.

The Hydrochloride.—3.5 g. of the quaternary salt were dissolved in absolute alcohol containing an excess of dry hydrochloric acid and treated with dry ether until a faint turbidity persisted. On rubbing and letting stand 3.2 g. of the hydrochloride separated slowly as pale yellow, radiating aggregates of rhombic crystals. When rapidly heated to 165°, then slowly, the salt begins to soften, and melts at 170–1° with gas evolution. It dissolves readily in methyl alcohol or chloroform, less easily in absolute alcohol, and only sparingly in hot, dry acetone, the insoluble portion changing to a gummy mass. As obtained above the hydrochloride apparently retains 2 molecules of water of crystallization. An attempt to drive this off at 80° *in vacuo*, resulted in the loss of hydrochloric acid.

Subs., 0.1487: 9.0 cc. N (22.5°, 765 mm.). Subs., 0.1201: 7.92 cc. $AgNO_3$ soln. (1 cc. = 0.001794 g. Cl).

Calc. for $C_{29}H_{36}O_4N_3Cl.HCl.2H_2O$: N, 7.03; Cl, 11.85. Found: N, 7.05; Cl, 11.83.

Hydroquinine Chloroacetyl-*p*-anisidine.—After boiling off the acetone the residue was taken up in hot commercial butyl alcohol. The filtrate deposited radiating masses of delicate needles and the separation was completed by the cautious additon of dry ether. The salt was recrystallized by dissolving in dry acetone, adding ligroin until the initial turbidity just dissolved, and seeding. When air-dry it retained an amount of solvent equivalent to between 1 and 1.5 molecules of water of crystallization. The anhydrous salt gradually softens to a jelly above 150° and is completely fluid at about 190°. $[\alpha]_D^{20} = -93.9°$ in absolute alcohol, $c = 1.128$. The salt dissolves very readily in methyl or ethyl alcohol or chloroform, somewhat less easily in dry acetone, and very sparingly in dry ether. It is difficultly soluble in cold water or benzene, readily on boiling, and separates from the former as a jelly on cooling. It dissolves in conc. sulfuric acid with a dull yellow color.

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[1] THIS JOURNAL, 41, 1452 (1919).

Subs. (anhydrous), 0.1424 10 0 cc N (18 5°, 745 mm.) Subs, 0 1461. 5 20 cc. $AgNO_3$ soln (1 cc = 0 00181 g Cl)

Calc. for $C_{29}H_{36}O_4N_3Cl$· N, 7 99; Cl, 6 75 Found N, 8 06; Cl, 6.45

The Hydrochloride.—The quaternary salt was dissolved in a small volume of absolute alcohol, treated with absolute alcoholic hydrochloric acid, and seeded with crystals obtained by manipulating a test portion with dry ether. The hydrochloride separated rapidly on rubbing as thick, yellow, hexagonal, microscopic plates. When rapidly heated to 180°, then slowly, the substance melts at 180–4° to an orange mass containing bubbles and becomes completely fluid and decomposes at about 190° It is rather sparingly soluble in the cold in absolute alcohol, easily on warming, and dissolves readily in dry methyl alcohol. The aqueous solution foams readily.

Subs., 0.1051: 7.40 cc. $AgNO_3$ soln. (1 cc = 0.001794 g Cl).

Calc. for $C_{29}H_{36}O_4N_3Cl.HCl$: Cl, 12.61. Found: 12.64.

Hydroquinine Chloroacetyl-*o*-phenetidine, $C_{20}H_{26}O_2N_2.ClCH_2CONH$-$C_6H_4OC_2H_5$(*o*-).—In the case of chloroacetyl-*o*-phenetidine[1] the acetone was boiled off and the residue taken up in boiling water and treated with boneblack. As the salt separated from the filtrate as an oil on rapid chilling it was necessary to cool slowly and seed with crystals obtained by adding sodium chloride to a diluted test portion. Recrystallized from water it separates very slowly on seeding as rosets and sheaves of delicate needles containing 2.5 molecules of water of crystallization. Additional quantities were recovered by treating the mother liquors carefully with saturated salt solution. The anhydrous salt softens above 125°, forms a transparent jelly at about 140° and a yellow fluid at 170–2°. It dissolves readily in methyl or ethyl alcohol, chloroform, or acetone, and only very sparingly in dry ether.

Subs. (air-dry), 0.7096: loss, 0.0573 *in vacuo* at room temp. over H_2SO_4.

Calc. for $C_{30}H_{38}O_4N_3Cl.2.5H_2O$: H_2O, 7.70. Found: 8.08.

Subs. (anhydrous), 0.1531: 11.0 cc. N (23.5°, 744 mm.). Subs., 0.1317: 4.45 cc $AgNO_3$ soln. (1 cc. = 0.001794 g. Cl).

Calc. for $C_{30}H_{38}O_4N_3Cl$: N, 7 79; Cl, 6.57 Found: N, 8.10; Cl, 6.07

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[1] THIS JOURNAL, 41, 1452 (1919)

Hydroquinine Chloroacetyl-*m*-phenetidine Hydrochloride.—(From 2.2 g. of chloroacetyl-*m*-phenetidine[1]) As the quaternary salt itself could not be obtained crystalline the acetone was boiled off and the residue taken up in absolute alcohol and treated with an excess of absolute alcoholic hydrochloric acid. The salt crystallized after adding dry ether to incipient turbidity and rubbing. The supernatant solution was then decanted off and the precipitate washed twice by decantation with dry alcohol-ether mixture containing a little hydrochloric acid. After dissolving the residue in boiling absolute alcohol, filtering hot from traces of impurities and adding a little absolute alcoholic hydrochloric acid, the salt separated when seeded as lemon-yellow, rhombic crystals, which are hygroscopic when moist. 4.2 g. were obtained, melting at 173–4° with preliminary sintering and softening. As so obtained the hydrochloride apparently retained 2 molecules of water of crystallization or one molecule of alcohol. It dissolves readily in water, a concentrated solution soon setting to a jelly. It also dissolves readily in chloroform and lightens in color and turns pasty under boiling dry acetone, possibly owing to dehydration. It dissolves sparingly in cold absolute alcohol, more easily on warming.

Subs., 0.1428: 8.3 cc. N (22.0°, 773 mm.). Subs., 0.1261: 8.15 cc. $AgNO_3$ soln. (1 cc. = 0.001794 g. Cl).

Calc. for $C_{30}H_{38}O_4N_3Cl.HCl.2H_2O$: N, 6.87; Cl, 11.58. Found: N, 6.85; Cl, 11.60.

Hydroquinine Chloroacetyl-*p*-phenetidine.—After removing the acetone the residue was taken up in boiling water, treated with boneblack, and the filtrate seeded with crystals obtained by slow, spontaneous evaporation of a test portion of the original solution. The salt was recrystallized from water, forming sheaves of delicate needles containing 2.5 molecules of water of crystallization, dissolving with difficulty in water, and giving $[\alpha]_D^{27.5} = -89.1°$ in 95% alcohol, $c = 1.033$. The anhydrous salt softens slightly above 110°, sinters to a jelly at 150–60°, turns yellow, slowly evolve gas, and becomes more fluid as the temperature is further raised, and is completely molten at 210°. It is very easily soluble in absolute alcohol, acetone, chloroform, or benzene, and only difficultly in dry ether. It gives a straw-yellow solution in conc. sulfuric acid.

Subs. (air-dry), 0.4068: loss, 0.0297 *in vacuo* at 80° over H_2SO_4.

Calc. for $C_{30}H_{38}O_4N_3Cl.2.5H_2O$: H_2O, 7.70. Found: 7.30.

Subs. (anhydrous), 0.1229: 8.85 cc. N (29.5°, 759 mm.). Subs., 0.1507: 5.62 cc. $AgNO_3$ soln. (1 cc. = 0.00181 g. Cl).

Calc. for $C_{30}H_{38}O_4N_3Cl$: N, 7.79; Cl, 6.57. Found: N, 8.11; Cl, 6.75.

Hydroquinine 4-Chloroacetylamino-guaiacol, $C_{20}H_{26}O_2N_2.4,5\text{-}HO(CH_3O)C_6H_3NHCOCH_2Cl$.—In the case of 4-chloroacetylamino-guaiacol[2] the acetone was poured off from the gummy product and this taken up in a relatively large volume of boiling water and treated with bone black. The practically colorless filtrate gradually darkened on standing, depositing the salt at the same time from the still warm solution as delicate, felted, almost colorless needles containing 2 molecules of water of crystallization. It is very difficultly soluble in cold water, fairly readily on boiling, and, judging by the low halogen figure obtained on analysis, appears to be somewhat hydrolyzed by this method of crystallization. An aqueous suspension gives a slowly developing orange color with ferric chloride. The anhydrous salt forms a brown jelly above 160°, becomes semifluid at about 190°, and is completely fluid and partially decomposed at 215°. It dissolves readily in methyl or ethyl alcohol or chloroform, and is difficultly soluble in boiling dry acetone, almost insoluble in boiling benzene It dissolves in conc. sulfuric acid with a pale greenish yellow color.

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[1] This Journal, 41, 1452 (1919).

[2] *Ibid.*, 41, 1457 (1919).

Subs (air-dry), 0.6924 loss, 0.0444 *in vacuo* at 80° over H_2SO_4

Calc for $C_{29}H_{36}O_5N_3Cl\,2H_2O$. H_2O, 6.24 Found 6.43

Subs (anhydrous), 0.1269 8.6 cc N (22.0°, 757 mm) Subs, 0.1832 AgCl, 0.0415.

Calc for $C_{29}H_{36}O_5N_3Cl$ N, 7.76, Cl, 6.55 Found N, 7.81, Cl, 5.61

Hydroquinine 3,4-Methylenedioxy-chloroacetanilide, $C_{20}H_{26}O_2N_2$.-3,4-$CH_2O_2C_6H_3NHCOCH_2Cl$.—Starting with 2.2 g. of 3,4-methylenedioxy-chloroacetanilide[1] the reaction mixture deposited the crystalline salt on standing. Recrystallized from dry methyl ethyl ketone it separated as sheaves of long, delicate needles. These were warmed slightly and evacuated to remove adhering solvent and allowed to come to equilibrium in the air, retaining one molecule of water of crystallization or its equivalent The yield was 1.5 g. The salt dissolves appreciably in cold water, quite readily on boiling, the solution forming a jelly on cooling and depositing a portion of the substance on standing as rosets of delicate needles. The anhydrous salt gradually melts, with slight preliminary softening, above 155-60°, turning orange and slowly evolving gas, and becoming completely fluid at 185°. It dissolves readily in methyl or ethyl alcohol, or chloroform, less easily in dry acetone. It gives a lemon-yellow color with conc. sulfuric acid.

Subs (air-dry), 0.5956 loss, 0.0195 *in vacuo* at 80° over H_2SO_4

Calc for $C_{29}H_{34}O_6N_3Cl\,H_2O$ H_2O, 3.23. Found. 3.29

Subs. (anhydrous), 0.1275 8.6 cc N (20.0°, 757 mm). Subs, 0.1527: AgCl, 0.0398

Calc for $C_{29}H_{34}O_6N_3Cl$ N, 7.79, Cl, 6.57 Found. N, 7.83; Cl, 6.45.

Hydroquinine 3,4-Dimethoxy-chloroacetanilide.—(From 2.3 g. of 3,4-dimethoxy-chloroacetanilide.[2]) The salt crystallized on standing and was dissolved in hot, dry acetone, filtered with the aid of boneblack, and the filtrate cautiously treated with ligroin, shaking to redissolve the gelatinous precipitate first formed. On seeding and letting stand overnight the salt separated as masses of hair-like needles and diamond-shaped plates containing solvent of crystallization. The yield was 3.1 g., an additional quantity, though less pure, separating from the mother liquors on standing. The anhydrous salt gradually softens and melts above 130° with gas evolution, becoming transparent at about 175° and completely fluid with decomposition at 205–10°. It softens under and dissolves readily in dry methyl or ethyl alcohol, dry chloroform, less readily, but freely in dry acetone. It is difficultly soluble in cold water, readily on heating, the solution gelatinizing on cooling. It dissolves with a yellow color in dil. hydrochloric or conc. sulfuric acid.

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[1] THIS JOURNAL, 41, 1457 (1919).

[2] *Ibid.*, 41, 1461 (1919)

Subs. (anhydrous), 0.1347. 9 4 cc. N (21.0°, 765 mm). Subs , 0.1237: 4 25 cc $AgNO_3$ (1 cc. = 0 001794 g. Cl).

Calc for $C_{30}H_{38}O_5N_3Cl$· N, 7 57; Cl, 6 38 Found. N, 8.16; Cl, 6 17.

Hydroquinine *m*-Chloroacetylamino-benzenesulfonamide, $C_{20}H_{26}O_2N_2.-ClCH_2CONHC_6H_4SO_2NH_2$(*m*-).—Using *m* - chloroacetylamino - benzenesulfonamide[1] the reaction mixture deposited a portion of the quaternary salt as a gum. This was dissolved by adding 1/2 volume of absolute alcohol, after which the salt soon began to separate. Recrystallized from dry methyl alcohol it forms faintly pinkish, glistening, hexagonal platelets which gradually soften to a jelly above 180°, darkening, and finally decomposing slowly at 200–5°. Aqueous suspensions dissolve on boiling or on adding dil. acid or alkali. The salt is difficultly soluble in cold dry methyl or ethyl alcohol, more easily on boiling, and is also somewhat soluble in boiling dry acetone and practically insoluble in boiling dry chloroform.

Subs. (anhydrous), 0.0926: 8.0 cc. N (26.0°, 770 mm.). Subs., 0.1961: AgCl, 0.0468.

Calc. for $C_{28}H_{35}O_5N_4ClS$: N, 9.75; Cl, 6.1.7 Found: N, 9.99; Cl, 5.90.

(F) Quaternary Salts of Hydroquinidine.

Hydroquinidine Chloroacetamide.—Hydroquinidine iodoacetamide was prepared in almost quantitative yield by suspending the finely pulverized base in hot acetone and adding one equivalent of iodoacetamide in small portions, the alkaloid going into solution as the reaction proceeded. After boiling for a few moments the salt began to separate as glistening hexagonal plates and was converted into the chloride as were its previously discussed isomers and analogs. The chloride was salted out from the aqueous solution and recrystallized from a small volume of water, forming aggregates of minute leaflets containing 5 molecules of water of crystallization and dissolving readily in water at room temperature, rather sparingly at 0°. The yield was about 1/2 the amount of quaternary iodide used. The anhydrous salt gradually softens up to 185° to a yellow jelly which becomes completely fluid and decomposes at 210°. $[\alpha]_D^{26} = +179.9°$ in water, $c = 1.078$. It dissolves readily at room temperature in methyl or ethyl alcohol, chloroform or acetone, and less easily in benzene.

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[1] This Journal, 39, 2429 (1917).

Subs. (air-dry), 0 8437· loss, 0.1443 *in vacuo* at room temp, then at 80° over H_2SO_4

Calc. for $C_{22}H_{30}O_3N_3Cl\ 5H_2O$ H_2O, 17 67 Found 17 11

Subs (anhydrous), 0 1305. 11 5 cc N (29 0°, 763 mm) Subs, 0 1572· 7 16 cc. $AgNO_3$ soln (1 cc = 0 00181 g Cl)

Calc. for $C_{22}H_{30}O_3N_3Cl$ N, 10 02, Cl, 8 45 Found N, 10 0; Cl, 8 25

Hydroquinidine *p*-Chloroacetylamino-phenol.—A suspension of the components in dry acetone soon cleared on boiling and after $^1/_2$ hour the salt suddenly crystallized and the mixture was allowed to stand in a warm place for 4 hours The yield was 83% of the theoretical amount. Recrystallized by dissolving in hot absolute alcohol, adding about 3 volumes of dry ether, and seeding, the salt forms rosets of delicate needles which darken and soften slightly when heated and melt only when kept in the bath at 285° for a few moments. It is very difficultly soluble in boiling water and practically insoluble in dry chloroform or acetone, but dissolves at room temperature in absolute alcohol, more easily in dry methyl alcohol.

Subs 0.1129. 8.4 cc N (27 0°, 758 mm) Subs, 0 1668 AgCl, 0 0460

Calc for $C_{28}H_{34}O_4N_3Cl$ N, 8 21, Cl, 6 93 Found N, 8 45, Cl, 6.82

The Hydrochloride.—The quaternary salt, rubbed under a small volume of 10 % hydrochloric acid, formed a gummy mass which crystallized on standing. A solution of the salt in hot water containing a few drops of dil. hydrochloric acid was cooled and treated with the conc. acid until the initial turbidity barely redissolved on stirring. On seeding and letting stand in the cold the hydrochloride separated as faintly yellow, minute rhombs which deliquesced rapidly in the warm, moist room. The dried salt does not have this objectionable property. It melts and decomposes at 245–50° with preliminary darkening and dissolves rather sparingly in cold water. It dissolves in dry methyl alcohol, sparingly in absolute alcohol, and is almost insoluble in boiling dry chloroform or acetone.

Subs 0 2039· AgCl, 0.1050.

Calc for $C_{28}H_{34}O_4N_3Cl\ HCl$ Cl, 12 93 Found. 12 74

Hydroquinidine Chloroacetyl-*p*-anisidine.—This salt was prepared in the same way and in the same yield as hydroquinidine-*p*-chloroacetylamino-phenol. Recrystallized from 25% alcohol it forms rosets of flat, cream-colored prisms which melt and decompose at 260–5°. It dissolves in dry chloroform and appreciably in methyl alcohol. It is sparingly soluble in absolute alcohol, more easily on boiling, and only very difficultly soluble in boiling water or dry acetone. It is optically inactive in dry chloroform, where $c = 1.019$.

Subs., 0.1110: 8.0 cc. N (26.0°, 765 mm.). Subs., 0.1209: 4.5 cc. $AgNO_3$ soln. (1 cc. = 0.00181 g. Cl).

Calc. for $C_{29}H_{36}O_4N_3Cl$: N, 7.99; Cl, 6.75. Found: N, 8.28; Cl, 6.74.

The Hydrochloride.—3 g. of the quaternary salt were dissolved in a few cc. of conc. hydrochloric acid and the solution then treated with small amounts of dry acetone, with shaking, until the volume was about 50 cc. On letting stand and rubbing occasionally the salt crystallized as faintly yellow, nacreous, rounded scales, crystallization being facilitated by the addition of more dry acetone and ether. The dried product, when rapidly heated to 195°, then slowly, melts and decomposes at 196–200°. It dissolves readily in water, methyl or ethyl alcohol, less easily in dry chloroform, and very difficulty in dry acetone.

Subs., 0.1148: 7.64 cc. $AgNO_3$ soln. (1 cc. = 0.00181 g. Cl).

Calc. for $C_{29}H_{36}O_4N_3Cl.HCl$: Cl, 12.61. Found: 12 05.

(G) Quaternary Salts of Hydrocupreine.

Hydrocupreine Chloroacetanilide Hydrochloride.—As hydrocupreine showed only very little tendency to combine with chloroacetanilide in boiling dry acetone it was found necessary to use iodoacetanilide, combining the substances in hot alcoholic solution. As the iodide showed no tendency to crystallize the solution was diluted until just turbid and shaken with freshly precipitated silver chloride. Most of the alcohol was removed from the filtrate by concentration *in vacuo* and after dilution with hot water and treating with boneblack the clear yellow filtrate was treated with saturated sodium chloride solution, precipitating the chloride as an amorphous, yellow solid. This was collected and rubbed up with conc. hydrochloric acid, changing to a faintly yellow mass of spherules of microscopic needles, which were filtered off after dilution with a little more than an equal volume of water. When rapidly heated to 210°, then slowly, it melts and decomposes at 213–4°. It dissolves readily in dry methyl alcohol, less easily in cold water or absolute alcohol, and is almost insoluble in dry chloroform or acetone.

Subs., 0.1428: 10.0 cc. N (21.5°, 759 mm). Subs., 0.1566: AgCl, 0.0888.

Calc. for $C_{27}H_{32}O_3N_3Cl.HCl$: N, 8.11; Cl, 13.68. Found: N, 8.11; Cl, 14.03.

Hydrocupreine Chloroacetyl-*p*-anisidine Hydrochloride.—3.3 g. of hydrocupreine, 2 g. of anhydrous sodium iodide, and 2 g. of chloroacetyl-*p*-anisidine were boiled for one hour in dry acetone. The base quickly dissolved and was replaced by a heavy precipitate of sodium chloride. The filtrate and washings were diluted with water and shaken for 45 minutes with freshly precipitated silver chloride. After adding an excess of hydrochloric acid to the filtrate it was concentrated to small bulk *in vacuo*, the last portions of the salt separating as colorless, hair-like needles. After washing with a little 10% hydrochloric acid the residue was dried *in vacuo*, dissolved in boiling absolute alcohol containing a little dry hydrochloric acid, cooled, and seeded with crystals obtained by rubbing a portion of the crude salt with absolute alcohol. The pure salt forms radiating masses of minute, pale yellow needles, which, after drying as usual melt to an orange jelly at 203–5.5° and become completely fluid, with gas evolution and darkening, at about 210°. It dissolves easily in water or methyl alcohol, slowly but freely in dry chloroform, and is appreciably soluble in absolute alcohol at room temperature, readily on warming. An aqueous solution gives a pale brownish color with ferric chloride.

Subs., 0.1205: 8.4 cc. N (24.5°, 750 mm.). Subs., 0.1088: 7.8 cc. $AgNO_3$ soln. (1 cc. = 0.001794 g. Cl).

Calc. for $C_{28}H_{34}O_4N_3Cl.HCl$: N, 7.67; Cl, 12.93. Found: N, 7.89; Cl, 12.86.

(H) Quaternary Salts of Ethylhydrocupreine.

Ethylhydrocupreine Methochloride.—The methiodide[1] in aqueous suspension, was quantitatively converted into the chloride in the usual manner. Recrystallized from water it forms aggregates of silky needles containing 2.5 molecules of water of crystallization and is rather difficultly soluble in cold water. The anhydrous salt softens when heated, melting to a paste at about 160°, then turning yellow and finally melting completely to an orange liquid filled with bubbles at 198–9°. $[\alpha]_D^{22} = -176.7°$ in water, $c = 0.651$. It dissolves readily in dry methyl or ethyl alcohol or dry chloroform, less easily in dry acetone.

Subs. (air dry), 0.6166: loss, 0.0633 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{22}H_{31}O_2N_2Cl.2.5H_2O$: H_2O, 10.33. Found: 10.27.
Subs. (anhydrous), 0.2442: AgCl, 0.0902.
Calc. for $C_{22}H_{31}O_2N_2Cl$: Cl, 9.07. Found: 9.14.

Ethylhydrocupreine Iodoacetamide.—Ethylhydrocupreine and iodoacetamide reacted quickly in acetone solution. Most of the acetone was evaporated off and the residue dissolved in hot water, the iodide separating in almost quantitative yield on cooling and rubbing. Recrystallized twice from water, using boneblack, it forms rosets of needles and long, narrow plates containing 3 molecules of water of crystallization. The anhydrous substance softens to a jelly at 140–50°, gradually liquefying and darkening, and becoming completely fluid at about 185°. $[\alpha]_D^{26} = -115.4°$ in absolute alcohol, $c = 0.910$. It dissolves readily in methyl or ethyl alcohol, chloroform or acetone.

Subs. (air-dry), 0.5403: loss, 0.0501 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{23}H_{32}O_3N_3I.3H_2O$: H_2O = 9.33. Found: 9.27.
Subs. (anhydrous), 0.1611: AgI, 0.0709.
Calc. for $C_{23}H_{32}O_3N_3I$: I, 24.17. Found: 23.78.

Ethylhydrocupreine Chloroacetamide.—The iodide was converted into the chloride and salted out with sodium chloride. Recrystallized from water it forms faintly yellow aggregates of long, narrow plates containing a little over 3 molecules of water of crystallization and dissolving fairly readily in water. The anhydrous salt melts to a jelly at 145–60°, turns yellow, then orange, and becomes completely fluid at about 195°. $[\alpha]_D^{23} = -114.8°$ in water, $c = 1.124$. It dissolves readily in absolute alcohol.

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[1] THIS JOURNAL, 41, 825 (1919).

Subs. (air-dry), 0.6813 loss, 0.0815 *in vacuo* at 100° over H_2SO_4
Calc for $C_{23}H_{32}O_3N_3Cl.3H_2O$ H_2O, 11.08 Found 11.97
Subs (anhydrous), 0.0852 7.3 cc N (27.0°, 753 mm) Subs, 0.1705 7.68 cc $AgNO_3$ soln (1 cc = 0.00181 g Cl)
Calc for $C_{23}H_{32}O_3N_3Cl$ N, 9.69, Cl, 8.17 Found N, 9.66, Cl, 8.16.

Ethylhydrocupreine *p*-Chloroacetylamino-phenol.—The salt, prepared by the direct method, crystallized in good yield on letting stand. Recrystallized from dry methyl ethyl ketone it formed rosets of delicate needles which came to equilibrium in the air with one molecule of water of crystallization. When rapidly heated to 175°, then slowly, it melted at 178–82° to a jelly. $[\alpha]_D^{22} = -71.8°$ in absolute alcohol, $c = 0.844$. The salt dissolves readily in absolute alcohol and very difficultly in water or dry acetone It softens under dry chloroform and dissolves to some extent.

Subs (air-dry), 0.5319 loss, 0.0181 *in vacuo* at 100° over H_2SO_4
Calc for $C_{29}H_{36}O_4N_3Cl.H_2O$ H_2O, 3.31 Found 3.40
Subs (anhydrous), 0.1359 9.4 cc N (18.0°, 760 mm)
Calc for $C_{29}H_{36}O_4N_3Cl$ N, 7.99 Found 8.12

The Hydrochloride.—On rubbing with 1:1 hydrochloric acid the quaternary salt changed to a pasty mass which gradually crystallized. Its solution in hot water containing a little hydrochloric acid was cooled, treated with the concentrated acid until the initial turbidity barely redissolved, and seeded. The hydrochloride separated in the refrigerator as almost colorless rosets of delicate needles. The anhydrous salt darkens at about 185°, gradually melting to an orange liquid and evolving gas at 196–7°. It dissolves readily in water, methyl or ethyl alcohol, and is practically insoluble in dry acetone.

Subs, 0.1528 10.62 cc $AgNO_3$ soln (1 cc = 0.00181 g Cl)
Calc for $C_{29}H_{36}O_4N_3Cl.HCl$ Cl, 12.61 Found 12.58.

Ethylhydrocupreine Chloroacetyl-*p*-anisidine.—The salt was obtained crystalline by evaporation of the acetone solution. After recrystallization from methyl ethyl ketone the yield was 82.5% of the theory. Recrystallized from boiling water, in which it is only difficultly soluble, it separates as delicate, hair-like needles containing 1.5 molecules of water of crystallization. The anhydrous salt softens to a jelly at 145–55°, turning yellow and liquefying completely by the time 200° is reached. $[\alpha]_D^{25} = -69.0°$ in absolute alcohol, $c = 1.574$. It dissolves readily in methyl or ethyl alcohol or chloroform, more slowly in dry acetone. It gives a pale yellow color in conc. sulfuric acid.

Subs. (air-dry), 0.7569: loss, 0.0334 *in vacuo* at 80°, then 100° over H_2SO_4.

Calc. for $C_{30}H_{38}O_4N_3Cl.1.5H_2O$: H_2O, 4.41. Found: 4.77.

Subs. (anhydrous), 0.1533: 10.6 cc. N (25.0°, 767 mm.). Subs., 0.1188: 4.3 cc. $AgNO_3$ soln. (1 cc. = 0.00181 g. Cl).

Calc. for $C_{30}H_{38}O_4N_3Cl$: N, 7.79; Cl, 6.57. Found: N, 7.99; Cl, 6.56.

The Hydrochloride.—A solution of the quaternary salt in an excess of absolute alcoholic hydrochloric acid was concentrated to dryness *in vacuo* and the gummy residue digested in the flask with dry acetone, a portion dissolving. After several days the hydrochloride began to crystallize as prismatic needles and became entirely crystalline on rubbing and letting stand. When rapidly heated to 200°, then slowly, the dried salt darkens and sinters at 201–4° and melts and decomposes at 204–5°. It dissolves readily in methyl or ethyl alcohol and only incompletely in water, owing to hydrolysis.

Subs. 0.1374: 9.46 cc. $AgNO_3$ soln. (1 cc. = 0.00181 g. Cl).

Calc. for $C_{30}H_{38}O_4N_3Cl.HCl$: Cl, 12.30. Found: 12.47.

Ethylhydrocupreine Chloroacetyl-*p*-phenetidine.—Ligroin was added to the reaction mixture and the solution allowed to stand in the ice box with occasional rubbing, the salt crystallizing in a yield of 80% of the theoretical amount Recrystallized with the aid of boneblack from boiling water, in which it is sparingly soluble it separated on seeding as woolly masses of delicate needles containing 1.5 molecules of water of crystallization. The anhydrous salt softens to a jelly above 130°, gradually liquefying and turning yellow as the temperature is raised, until completely fluid, with slow decomposition at about 210°. $[\alpha]_D^{25.5} = -75.25°$ in 95% alcohol, $c = 0.917$. It dissolves extremely easily in chloroform, very readily in methyl or ethyl alcohol, and easily in dry acetone.

Subs. (air-dry), 0.5089: loss, 0.0232 *in vacuo* at 80°, then 100° over H_2SO_4.

Calc. for $C_{31}H_{40}O_4N_3Cl.1.5H_2O$. H_2O, 4.65. Found: 4.56.

Subs. (anhydrous), 0.1198: 8.25 cc. N (27.0°, 762 mm.). Subs., 0.1276: 4.47 cc. $AgNO_3$ soln. (1 cc. = 0.00181 g Cl).

Calc. for $C_{31}H_{40}O_4N_3Cl$: N, 7.59, Cl, 6.40. Found: N, 7.86; Cl, 6.35.

The Hydrochloride.—This salt was obtained in exactly the same way as the corresponding anisidine compound, forming aggregates of minute, thick plates with tapering ends. It begins to turn yellow above 150°, darkens at about 200°, then softens and sinters, and melts and decomposes at 208°. It softens under water and dissolves slowly but completely on shaking. It is also readily soluble in absolute alcohol or chloroform and only very sparingly in dry acetone.

Subs., 0.1357: 8.7 cc. N (25.0°, 750 mm.). Subs., 0.1415: 9.42 cc. $AgNO_3$ soln. (1 cc. = 0.00181 g. Cl).

Calc. for $C_{31}H_{40}O_4N_3Cl.HCl$: N, 7.12; Cl, 12.02. Found: N, 7.25; Cl, 12.05.

NEW YORK, N. Y

[CONTRIBUTION FROM THE ESSENTIAL OILS LABORATORY, DRUG DIVISION, BUREAU OF CHEMISTRY, U. S. DEPARTMENT OF AGRICULTURE.]

VANILLYL-ACYL AMIDES.

BY E. K. NELSON.

Received October 2, 1919

The investigation in this laboratory of the constitution of capsaicin,[1] which demonstrated that substance to be a vanillyl-decenoyl amide, has led to the synthesis of a number of other vanillyl-acyl amides (4-hydroxy-3-methoxy-benzyl-acyl amides), of the type $(4)HO(3)CH_3OC_6H_3(1)CH_2$-NHCOR.

Vanillyl amine, suspended in dry ether, reacts readily with acyl chlorides, forming vanillyl-acyl amides, which are substances of the capsaicin type.

General Method of Preparation.

A quantity of vanillyl amine corresponding to two molecules, freed from its water of crystallization by heating at 110°, is suspended in dry ether, and a quantity of the acyl chloride corresponding to one molecule is added, the mixture being stirred meanwhile. The mixture is then heated gently to complete the reaction, water and a little hydrochloric acid are added, and the mixture is shaken out in a separatory funnel, the aqueous layer being drawn off. In case acids of low molecular weight, up to hexoic acid, are being used, it is necessary to extract the aqueous solution thoroughly with chloroform and add this to the ether solution, as the derivatives of the lower acids are soluble in water and insoluble, or difficultly soluble, in ether. The aqueous solution is then evaporated to recover the excess of vanillyl amine in the form of the hydrochloride. The ether or chloroform-ether solution is washed with a dilute solution of sodium carbonate, to remove any uncombined acid, and evaporated.

The condensation product thus obtained is purified by crystallizing from a suitable solvent, usually benzene for the lower members of the series, or petroleum ether containing some ethyl ether for the higher ones.

The acyl chlorides are prepared as needed by adding to the weighed amount of acid the required quantity of phosphorus trichloride, heating gently and decanting the acyl chloride directly from the viscous deposit of phosphorous acid.

The foregoing method of preparation was employed for all the substances to be described, with the exception of the acetyl and isobutyryl derivatives, which were made by the use of the corresponding acid anhydrides.

Derivatives of the Acids of the Acetic Acid Series.

Vanillyl Acetamide.—10 g. of vanillyl amine, 20 g. of acetic anhydride and one g. anhydrous sodium acetate were heated for 4 hours at 130°. An excess of sodium hydroxide was added to the cooled mixture and after shaking and saturation with carbon dioxide the solution was thoroughly extracted with chloroform. The residue from evaporation of the chloroform was saponified with cold alcoholic potassium hydroxide, in order to remove the acetyl group substituted in the hydroxyl of the vanillyl residue, diluted with water, saturated with carbon dioxide and extracted with chloroform. On evaporating the chloroform the compound remained as a thick brown syrup which slowly became crystalline. Recrystallized from boiling benzene it melted at 84–5° (corr.). The yield was 62%.

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[1] Nelson, THIS JOURNAL, 41, 1115 (1919).

Calc. for $C_{10}H_{13}NO_3$: C, 61.5; H, 6.7; N, 7.17.
Found: C, 61.6; H, 6.9; N, 7.12.

Vanillyl acetamide is easily soluble in water and in chloroform but is insoluble in ether. It is not pungent.

Optical-crystallographic Data[1]—*In ordinary light*, vanillyl acetamide is seen to consist of rods breaking into irregular fragments, the crystal system being monoclinic. The refractive indices (determined by the immersion method, using mixtures of lubricating oil with monobromonaphthalene and of the latter with methylene iodide) are: $\alpha = 1.550$, $\beta = 1.585$, $\gamma = 1.685$, $\gamma - \alpha = 0.135$, all ± 0.005. Intermediate values are usually obtained. *In parallel polarized light, nicols crossed:* The birefringence is extreme, the colors being of high orders. Extinction is inclined, reaching a maximum of 30°; elongation is variable. *In convergent polarized light, nicols crossed:* Partial biaxial figures are often obtained, the axial plane running lengthwise, the apparent axial angle 2E being about 110° (calc. 115°) and the sign positive. The dispersion is distinct.

Vanillyl Propionamide.—2.5 g. of propionic acid was converted into the chloride and added to 10.3 g. of vanillyl amine suspended in ether. The derivative was recrystallized from hot benzene and melted at 108–10° (corr.). The yield was 46%.

Calc. for $C_{11}H_{15}NO_3$: C, 63.1; H, 7.2; N, 6.69.
Found. C, 63.3; H, 7.2; N, 6.67.

Vanillyl propionamide is scarcely soluble in ether but is soluble in water, chloroform or hot benzene. Its aqueous solution is very slightly pungent.

Optical-crystallographic Data.—*In ordinary light*, vanillyl propionamide is in short rods and irregular grains, the system being rhombic. Refractive indices, determined as in the preceding substance: $\alpha = 1.495$, $\beta = 1.635$, $\gamma = 1.680$, $\gamma - \alpha = 0.185$, all ± 0.005; intermediate values are usually obtained. *In parallel polarized light, nicols crossed:* Birefringence is extreme, the colors being of high orders. Extinction is parallel, and elongation variable. *In convergent polarized light, nicols crossed:* Partial biaxial figures are occasionally obtained, 2E being about 100° (calc. 98°) and the sign negative. Dispersion is distinct.

Vanillyl *n*-Butyramide.—Normal butyric acid was used and the acid chloride method employed. The yield was 44%. Vanillyl *n*-butyramide crystallizes slowly. It was crystallized from benzene and recrystallized from dry ether, when it melted at 68–70° (corr.).

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[1] The optical-crystallographic observations in this paper were kindly made by Dr. Edgar T. Wherry, of the Bureau of Chemistry.

Calc for $C_{12}H_{17}NO_3$: C, 64.5, H, 7.7, N, 6.29
Found. C, 64.4, H, 7.6; N, 6.34

Vanillyl *n*-butyramide is readily soluble in chloroform and moderately soluble in ether and in water. It is somewhat pungent.

Optical-crystallographic Data.—*In ordinary light*, vanillyl *n*-butyramide is in minute rods, grains and irregular aggregates, the system being apparently triclinic. Refractive indices: $\alpha = 1.515$, $\beta = 1.580$, $\gamma = 1.655$, $\gamma - \alpha = 0.140$, all ± 0.005; intermediate values are usually obtained. *In parallel polarized light, nicols crossed* Birefringence is extreme, the colors being of high orders. Extinction is strongly inclined, reaching 45°, and elongation is variable. *In convergent polarized light, nicols crossed:* Partial biaxial figures are often obtained, 2E being extremely large, and the sign probably positive. Dispersion is distinct.

Vanillyl Isobutyramide.—Isobutyric anhydride was employed. The yield was 80%. Recrystallized from dil. alcohol, vanillyl isobutyramide melted at 118–20°.

Calc for $C_{12}H_{17}NO_3$ C, 64.5, H, 7.7, N, 6.29
Found C, 64.4, H, 7.7, N, 6.15

Vanillyl isobutyramide is scarcely soluble in ether but is soluble in chloroform and moderately soluble in water. It is only slightly pungent.

Optical-crystallographic Data.—*In ordinary light*, vanillyl isobutyramide is in rectangular plates and pyramids, the system being rhombic. Refractive indices: $\alpha = 1.465$, $\beta = 1.633$, $\gamma = 1.635$, $\gamma - \alpha = 0.170$, all ± 0.005. *In parallel polarized light, nicols crossed:* Birefringence is extreme, the colors being of high orders. Extinction is symmetrical, and elongation variable. *In convergent polarized light, nicols crossed:* Biaxial figures are often obtained, 2E being very small, about 18° (calc. 17° 48′), and the sign negative. Dispersion is distinct.

Vanillyl *n*-hexoylamide.—Caproic acid made by the fermentation of kelp was used in preparing vanillyl *n*-hexoylamide. The acid was obtained from the Hercules Powder Co., Although it distilled within narrow limits as received, it was converted into the methyl ester and this was carefully fractionated. The fraction boiling at 49–52° under 15 mm. pressure was saponified, and from this an acid boiling at 103–6° under 15 mm. pressure was obtained.

Vanillyl *n*-hexoylamide, however, was not obtained in crystalline form and all efforts to induce crystallization failed. It seems probable, therefore, that the caproic acid may not be pure normal acid. The condensation product, as obtained, appears as a light brown, very viscous syrup. It is moderately soluble in boiling water, from which it separates, for the most part, on cooling. It is soluble in ether and in chloroform. Vanillyl *n*-hexoylamide is far more pungent than the lower members of the series.

Vanillyl *n*-Heptoylamide.—Normal heptoic acid was made by the oxidation of oenanthol, which was prepared by distilling castor oil under diminished pressure. The acid boiled at 114° under 10 mm. pressure. By the condensation of *n*-heptoic acid and vanillyl amine, through the acid chloride, a yield of 81% of vanillyl *n*-heptoylamide was obtained. Recrystallized from a mixture of ether and petroleum ether, it melted at 59–61° (corr.).

Calc for $C_{15}H_{22}NO_3$: C, 67.9; H, 8 7; N, 5.24.
Found: C, 67.5, H, 8 7; N, 5.19

Vanillyl *n*-heptoylamide is very pungent.

Optical-crystallographic Data.—*In ordinary light,* vanillyl *n*-heptoylamide is in grains, the system being probably monoclinic. Refractive indices: $\alpha = 1.515$, $\beta = 1.595$, $\gamma = 1.625$, $\gamma - \alpha = 0.110$, all ±0.005; intermediate values are usually obtained. *In parallel polarized light, nicols crossed:* Birefringence is extreme, the colors being mostly about 3rd order. Extinction is usually strongly inclined, though occasionally symmetrical, and elongation is variable. *In convergent polarized light, nicols crossed:* Partial biaxial figures are occasionally obtained, 2E being about 110° (calc 107°), and the sign negative. Dispersion is distinct.

Vanillyl *n*-octoylamide.—Caprylic acid (normal octoic acid) was isolated from coconut oil by carefully fractionating the methyl esters of coconut oil fatty acids. The fraction boiling at 83–6° under 15 mm. pressure was saponified and the acid recovered and rectified.

As a perfectly homogeneous condensation product was not obtained with vanillyl amine, the acid was further purified by fractionally crystallizing its barium salt. The acid thus purified had a constant boiling point and was used in preparing vanillyl *n*-octoylamide, of which a yield of 83% was obtained. Recrystallized from petroleum ether containing 10% of ethyl ether, this compound melted at 41–3° (corr.).

Calc. for $C_{16}H_{25}NO_3$: C, 68 8; H, 9.0; N, 5.01.
Found: C, 68.8; H, 9.1; N, 5.05.

Vanillyl *n*-octoylamide is a violently pungent substance. Care must be taken in handling it that its solutions do not come in contact with the face or with the eyes. Its pungency on the tongue is about equal to that of capsaicin, but its property of causing sneezing and coughing is probably not quite so great.

Optical-crystallographic Data.—*In ordinary light,* vanillyl *n*-octoylamide is in very minute needles, with the approximate refractive indices $\alpha = 1.56$ and $\gamma = 1.57$. *In parallel polarized light, nicols crossed:* Birefringence is moderate, the colors being first order grays. Extinction is parallel and elongation negative. The grains are too minute for further measurements.

Vanillyl *n*-Nonoylamide.—Normal nonoic acid was purified by distillation. Condensed, through the acid chloride, with vanillyl amine, a yield of 76% of the theoretical equivalent of vanillyl *n*-nonoylamide was obtained. The substance crystallized slowly. Recrystallized from a mixture of ether and petroleum ether, it softened at 47° and was completely melted at 52°. It, therefore, still contained a small amount of impurities.

Calc. for $C_{17}H_{27}NO_3$: C, 69.6; H, 9.3; N, 4.77.
Found: C, 69.3; H, 9.1; N, 4.69.

Vanillyl *n*-nonoylamide is soluble in ether and in chloroform, and is slightly soluble in hot petroleum ether. It is an extremely pungent substance, being even more disagreeable to handle than vanillyl *n*-octoylamide. Its pungency to the taste is about the same as that of capsaicin.

Optical-crystallographic Data.—The optical properties of this substance are practically the same as those of vanillyl *n*-octoylamide, so far as they could be observed, except for the refractive indices, which are: $\alpha = 1.57$ and $\gamma = 1.59$.

Vanillyl *n*-Decoylamide.—Capric acid (normal decoic acid) was prepared by fractionation of the methyl esters of the coconut oil fatty acids. The methyl ester boiling at 112–6° under 15 mm. pressure was saponified and the acid recovered was crystallized and pressed out on filter paper in a cold room. The acid melted at 31–31.5°. A yield of 80% of vanillyl *n*-decoylamide was obtained. Recrystallized from petroleum ether, it melted at 59–60°.

Calc. for $C_{18}H_{29}NO_3$: C, 70.3, H, 9.5, N, 4.55.
Found: C, 70.1; H, 9.8; N, 4.58

Vanillyl *n*-decoylamide is soluble in chloroform and in ether and is slightly soluble in boiling petroleum ether and in water. It is extremely pungent and the powdered substance causes coughing and sneezing.

Optical-crystallographic Data.—*In ordinary light,* vanillyl *n*-decoylamide is made up of splintery flakes and needles, the system being probably rhombic. Refractive indices: $\alpha = 1.545$, $\beta = 1.555$, $\gamma = 1.620$, $\gamma - \alpha = 0.075$, all ± 0.005; β is usually seen lengthwise of the needles, and values intermediate between the other two indices crosswise. *In parallel polarized light, nicols crossed:* Birefringence is extremely strong, the colors being of upper first order, even on the thinner needles. Extinction is parallel and elongation usually negative, rarely positive. *In convergent polarized light, nicols crossed:* The crystals are too minute to yield good figures, but the class is biaxial, with the axial plane crosswise; 2E is small (calc. 23°) and the sign positive.

Vanillyl *n*-Undecoylamide.—An alcoholic solution of undecenoic acid, made by the dry distillation of castor oil, was hydrogenated, using colloidal palladium as a catalyst. 96% of the theoretical amount of hydrogen was quickly absorbed. The undecoic acid obtained was used in the preparation of vanillyl *n*-undecoylamide, of which a yield of 80% was obtained. Recrystallized from petroleum ether containing 10% of ethyl ether, the substance melted at 54–6°.

Calc for $C_{19}H_{31}NO_3$ C, 71.0, H, 9.7; N, 4.35
Found C, 71.1; H, 10.0, N, 4.44

Vanillyl *n*-undecoylamide is insoluble in water, difficultly soluble in cold petroleum ether and easily soluble in ether.

The pungency of vanillyl *n*-undecoylamide differs somewhat in character from that of the substances already described. The burning sensation is not so immediately apparent and affects the back of the tongue and the throat rather than the tip of the tongue

Optical-crystallographic Data.—*In ordinary light,* vanillyl *n*-undecoylamide is in 4-sided or irregular plates, the system being apparently triclinic. Refractive indices $\alpha = 1.515$, $\beta = 1.540$, $\gamma = 1.615$, $\gamma - \alpha = 0.100$, all ± 0.005; β is often obtained. *In parallel polarized light, nicols crossed:* Birefringence is extreme, the colors being of second order on even rather thin flakes. Extinction is inclined at varying angles, and elongation variable *In convergent polarized light, nicols crossed:* Partial biaxial figures are frequently obtained, 2E being about 110° (calc 106°) and the sign positive. Dispersion is distinct.

Vanillyl *n*-Dodecoylamide.—Lauric acid (normal dodecoic acid) was prepared by fractionating the methyl esters of coconut oil fatty acids. A yield of 70% of vanillyl *n*-dodecoylamide was obtained. It was recrystallized by pouring its ethereal solution into petroleum ether. It then melted at 60–1° (corr.).

Calc for $C_{20}H_{33}NO_3$ C, 71.6, H, 9.9; N, 4.17 Found C, 71.2, H, 10.2; N, 4.26

Vanillyl *n*-dodecoylamide is insoluble in water but easily soluble in ether. In pungency it resembles vanillyl *n*-undecoylamide.

Optical-crystallographic Data.—*In ordinary light,* vanillyl *n*-dodecoylamide is in splintery plates, the system being apparently monoclinic. Refractive indices. $\alpha = 1.52$, $\beta = 1.54$, $\gamma = 1.60$, $\gamma - \alpha = 0.08$, all ± 0.01. *In parallel polarized light, nicols crossed:* Birefringence is strong, the colors being 1st order yellow on even rather thin flakes. Extinction is inclined, reaching a maximum value of 30°, and elongation is negative. *In convergent polarized light, nicols crossed:* Rather indistinct figures are sometimes obtained, the class being biaxial, 2E moderate (calc. 100°) and sign positive.

Derivatives of the Acids of the Acrylic Acid Series.

Two derivatives of the acrylic acid series, to which the acid isolated from capsaicin belongs, have been made, namely, vanillyl crotonylamide and vanillyl undecenoylamide.

Vanillyl Crotonylamide.—The chloride of crotonic acid was prepared from crotonic acid by the method described by Henry,[1] and was used in the preparation of vanillyl crotonylamide, of which a 50% yield was obtained. Recrystallized from boiling benzene, the substance melted at 119–20° (corr.).

Calc for $C_{12}H_{15}NO_3$ C, 65.1; H, 6.8; N, 6.33 Found: C, 64.9, H, 7.0; N, 6.25.

Vanillyl crotonylamide is not easily soluble in ether or benzene but is quite soluble in chloroform and moderately soluble in water. It is slightly pungent.

Optical-crystallographic Data.—*In ordinary light,* vanillyl crotonylamide is in rods and irregular grains, the system being probably rhombic. Refractive indices: $\alpha = 1.515$, $\beta = 1.605$, $\gamma = 1.735$, $\gamma - \alpha = 0.220$, all ± 0.005; intermediate values are usually obtained. *In parallel polarized light, nicols crossed:* Birefringence is extreme, the strongest met with in the series studied, the colors being of high orders. Extinction is parallel, and elongation variable. *In convergent polarized light, nicols crossed:* Partial biaxial figures are occasionally obtained, 2E being extremely large, and the sign positive. Dispersion is distinct.

Vanillyl Undecenoylamide.—Undecenoic acid melting at 24.5° was obtained by the dry distillation of castor oil. Condensation with vanillyl amine gave a yield of 82% of vanillyl undecenoylamide. Purified by recrystallizing from petroleum ether, the substance melted at 53–5° (corr.).

Calc for $C_{19}H_{29}NO_3$: C, 71.4, H, 9.1, N, 4.38 Found C, 71.3; H, 9.3; N, 4.17

Vanillyl undecenoylamide, like the corresponding saturated derivative, vanillyl undecoylamide, affects the throat rather than the tongue. Its powder is more irritating to the nose and throat, however, causing violent coughing and sneezing.

Optical-crystallographic Data.—*In ordinary light,* vanillyl undecenoylamide is in splintery masses and minute needles, the system being probably rhombic. Refractive indices: $\alpha = 1.55$, $\beta = 1.60$, $\gamma = 1.63$, $\gamma - \alpha = 0.08$, all ± 0.01. *In parallel polarized light, nicols crossed:* Birefringence is extremely strong, first to second order colors being shown on even minute needles. The extinction is parallel and the elongation negative. *In convergent polarized light, nicols crossed:* The needles are too minute to yield good figures; the class is biaxial, 2E extremely large and the sign negative.

Derivatives of Aromatic Acids.

Of the aromatic acids, the derivative of benzoic acid is the only one so far successfully prepared. One effort to prepare a cinnamic acid derivative resulted in a product without a sharp melting point which is, therefore, not described.

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[1] Henry, *Bull. acad. roy. belg.*, [3] 36, 42 (1898).

Vanillyl Benzoylamide.—Vanillyl benzoylamide was made by stirring a quantity of benzoyl chloride corresponding to one molecule with a quantity of vanillyl amine corresponding to two molecules, suspended in dry ether. It crystallized from alcohol in needles melting at 140–2°.

Calc. for $C_{15}H_{15}NO_3$: C, 70.0; H, 5.9; N, 5.44. Found: C, 69.9; H, 6.0; N, 5.46.

Vanillyl benzoylamide is insoluble in ether but soluble in chloroform and alcohol. It is only moderately pungent.

Optical-crystallographic Data.—*In ordinary light,* vanillyl benzoylamide is in short rods and grains, the system being rhombic. Refractive indices: $\alpha = 1.590$, $\beta = 1.675$, $\gamma = 1.695$, $\gamma - \alpha = 0.105$, all ± 0.005; the individual indices are all frequently obtained. *In parallel polarized light, nicols crossed:* Birefringence is extreme, the colors being of high orders. Extinction is parallel, and elongation positive. *In convergent polarized light, nicols crossed:* Good biaxial interference figures are readily obtained, 2E being 85° (calc. 89°) and the sign negative. Dispersion is distinct.

Derivatives of *n*-valeric acid, of Wallach's "menthonensäure"[1] (a decenoic acid) and of Schneegans' decenoic acid[2] have been prepared, and were all found to be pungent substances. As none of them have crystallized, they cannot be described at present.

Pungency.

Capsaicin and the related substances described are practically devoid of odor and flavor.

The relative pungency of these substances was determined by ascertaining the minimum amount necessary to cause a distinct burning on the tip of the tongue.

It was found that $^1/_{8000}$ mg. of capsaicin could be detected by this means, and comparisons were made with that amount of capsaicin as a standard. An alcoholic solution of capsaicin was prepared of such a concentration that one drop from a pipet giving 80 drops to the cc. contained the required amount. One drop was evaporated on a small microscopic cover glass and placed on the tongue, and the intensity of the sensation and its duration noted.

Alcoholic solutions of the substances to be tested were diluted until the residue of a drop from the same pipet gave, as nearly as could be determined, the same degree of pungency. It is self-evident that such a comparison can only be approximate. The tests, therefore, were repeated by several persons, in order to eliminate, so far as possible, the personal equation. The results are expressed on a percentage scale, the pungency of capsaicin being taken as 100. The moderately pungent substances were not considered.

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[1] *Ann.*, 312, 197 (1900).

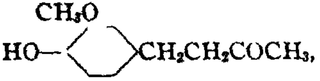
[2] *Ibid.*, 227, 85 (1885).

TABLE I.—COMPARATIVE PUNGENCIES.

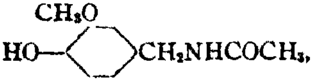
Vanillyl *n*-hexoylamide	5
Vanillyl *n*-heptoylamide	25
Vanillyl *n*-octoylamide	75
Vanillyl *n*-nonoylamide	100
Vanillyl *n*-decoylamide	50
Vanillyl *n*-undecoylamide	25
Vanillyl *n*-dodecoylamide	25
Vanillyl undecenoylamide	25

This method was checked by the method of Pearson,[1] *i. e.*, by dilution until pungency was barely perceptible when a few drops of the solutions were tasted.

Zingerone,[2] (4-hydroxy-3-methoxy-phenylethylmethyl ketone),



$HO-C_6H_3(OCH_3)-CH_2CH_2COCH_3$, one of the pungent principles of ginger, is far less pungent than capsaicin. A direct test upon the tongue, as described above, as well as a test by Pearson's method, showed it to have approximately one-thousandth the pungency of capsaicin. Vanillyl acetamide,



$HO-C_6H_3(OCH_3)-CH_2NHCOCH_3$, notwithstanding its structural similarity to zingerone, is not pungent

The property of pungency would seem to be, to some extent, dependent upon solubility. Zingerone is sparingly soluble in water and easily soluble in most of the organic solvents, with the exception of petroleum ether. It thus corresponds with the more pungent of the vanillyl-acyl amides. Vanillyl acetamide, on the other hand, is quite soluble in water, but difficultly soluble in ether.

Backman[3] shows that, in order for a substance to be odorous, it must be sufficiently soluble in both water and lipoids, since the cells of the nose are covered with a watery fluid, while they themselves contain lipoid granules.

Durrans,[4] in a valuable paper on the relationship between odor and chemical constitution, concludes that "a high molecular weight undoubtedly suppresses an odor, but a moderate molecular weight increases it." The following table, given by Durrans, expresses this relation:

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[1] *Pharm. J.*, 103, 78 (1919).

[2] Nomura, *J. Trans. Chem. Soc.*, 111, 769 (1917). Lapworth, *et al.*, *J. Trans. Chem. Soc.*, 111, 777, 790 (1917).

[3] *J. physiol. path gen.*, 17, 1 (1917).

[4] *Perfumery Essent. Oil Record*, 10, 104 (1919).

RELATION BETWEEN MOLECULAR WEIGHT AND INTENSITY OF ODOR.

	Odor develops	Maximum odor	Odor lost
Aliphatic saturated alcohols	C_6	C_8	C_{14}
Aliphatic saturated aldehydes	C_1	C_{10}	C_{16}
Aliphatic saturated ketones.	C_8	C_{11}	C_{16}
Aliphatic saturated acids	C_1	C_6	C_{14}
Aliphatic saturated esters	C_4	C_8	C_{17}

In the absence of a scientific method for the classification and measurement of odors, any attempt, such as the above, to correlate odor with chemical constitution must necessarily be largely empirical. It is, however, interesting to note that the increase in pungency to a maximum and subsequent decrease with increasing molecular weight would seem to run closely parallel with the variations of odor in series of organic substances brought out by Durrans

Summary and Conclusions.

The condensation products of vanillyl amine with acetic, propionic, butyric, isobutyric, *n*-hexoic, *n*-heptoic, *n*-octoic, *n*-nonoic, *n*-decoic, *n*-undecoic, *n*-dodecoic, crotonic, undecenoic and benzoic acids have been prepared and described.

In the homologous series of the derivatives from saturated fatty acids, the solubility in water decreases with rising molecular weight, while the solubility in ether increases, whereas pungency increases until it reaches a maximum in vanillyl *n*-nonoylamide, then decreases or changes in character as the molecular weights increase.

Conclusions as to the effect of a double bond in the side chain cannot at present be drawn, as only two derivatives of the acrylic acid series have been prepared. Comparison of one of these (vanillyl undecenoylamide) with the corresponding saturated derivative, however, seems to indicate that the double bond may not increase the pungent taste but may increase the other irritating properties.

WASHINGTON, D C.

[Contribution from the Laboratories of the Rockefeller Institute for Medical Research.]

SYNTHESES IN THE CINCHONA SERIES. III. AZO DYES DERIVED FROM HYDROCUPREINE AND HYDROCUPREIDINE.

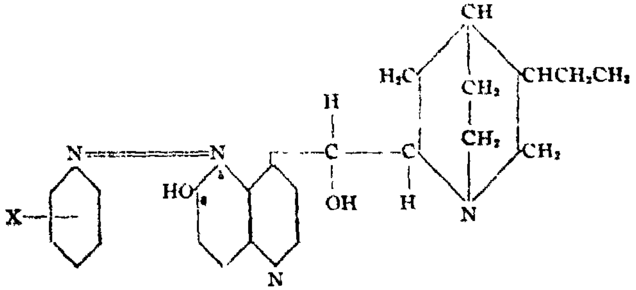
By Michael Heidelberger and Walter A. Jacobs.

Received October 6, 1919

The subject matter of this and the previous paper (p. 2090) was presented at the June meeting of the New York Section of the American Chemical Society. Three months later, while the present material was being prepared for publication we received the paper of Giemsa and Halberkann[1] on "Azo-5 and Amino-5 Compounds of Cupreine, Hydrocupreine and their Methyl and Ethyl Ethers," in which the idea of azo-cinchona compounds is elaborated, although only one of the substances described in the present paper (*p*-sulfo-phenylazo-hydrocupreine) was studied. The work which we now report has been in progress for over two years and represents but a portion of the studies which we are making in the field of the cinchona alkaloids.[2] Among our objects in studying the azo derivatives of the hydroxy alkaloids was the reduction of suitable members to the amino alkaloids, which we now see has also been accomplished by the German workers. As far as 5-aminohydrocupreine is concerned, we, too, prepared this interesting compound almost two years ago, and since our work with it and analogous substances is still in progress, we shall reserve our discussion of the amino alkaloids for a future paper.

We have found that hydrocupreine and hydrocupreidine behave in a normal manner as phenolic compounds and yield well-defined azo dyes with diazotized aromatic amines.

We have assumed from the first that position 5 (*ana*) in the quinoline nucleus is the place of entrance of the azo group



since this is the only available position which would satisfy the usual rules of substitution for a 6-hydroxy-quinoline derivative, a conclusion also arrived at by Giemsa and Halberkann.

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[1] *Ber.*, 52, 906 (1919).

[2] For Paper I of this series, see This Journal, 41, 818 (1919).

Of the dyes prepared by us from a large variety of aromatic amines the majority crystallized without difficulty or formed crystalline salts, and while others could not be made to crystallize we are convinced that methods for their crystallization could have been found in a more detailed and time-consuming study than we were able to give. In general, the phenyl and tolyl dyes, as well as those with *m*-substituents on the benzene ring gave orange to orange-red solutions in dil. acids and dyed silk various shades of orange; *o*- and *p*-alkoxy groups deepened these colors toward the red, while the dyes from the naphthylamines dyed silk a deep rose color. As a class these substances had the property of dyeing unmordanted cotton, a property also shared by 5-phenylazo-6-hydroxyquinoline,[1] which was prepared for comparison.

While the crystalline dyes which did not contain negative salt-forming groups on the aromatic amine were generally only slightly soluble in cold *N* aqueous alkali and only incompletely on boiling, solutions of the dyes in a little alcohol gave clear, deep red to purplish red solutions on dilution with *N* sodium hydroxide. All of the dyes, of course, were soluble in dil. acids.

Many of the substances described in this paper were highly bactericidal *in vitro*, a property which will be discussed in the appropriate place by our colleague, Dr. Martha Wolstein.

Experimental.

Since the azo compounds to be described in the following pages were all prepared by essentially the same technique this will be given at the start, and in cases in which modifications proved necessary these will be described under the individual compounds.

The aromatic amine was diazotized as usual in dil. hydrochloric acid solution containing 4 equivalents of the acid. The solution was then slowly added to a turbined solution of hydrocupreine in dil. sodium hydroxide, the quantity of the latter being 6 equivalents, or 2 in excess of the amount of hydrochloric acid originally employed, this having been chosen in order to hold the alkaloid in solution during the coupling. The volume of the alkaline solution was from 100 to 150 cc. for 3.1 g. (0.01 mol.) of the base and the temperature during the coupling was kept at 10–15°. As a rule the coupling proceeded rapidly, the dye in most cases separating during the reaction as a flocculent precipitate. In most instances precipitation was completed by the final addition of ammonium chloride solution. After filtering off and washing, the dye was purified by grinding under very dilute hydrochloric acid, filtering from insoluble material, and reprecipitating from the diluted filtrate with ammonia.

(A) Dyes Derived from Hydrocupreine.

Phenylazo-hydrocupreine.—On adding insufficient ammonia for neutralization to the dil. hydrochloric acid solution of the crude product a tarry precipitate which separated was filtered off before making alkaline with ammonia. The dye was obtained in slightly greater yield than the amount of hydrocupreine used and forms an orange-red, amorphous powder which is readily soluble in the usual organic solvents It gradually softens above 85°, melting completely at about 130°. It is soluble in dil acids with an orange color and although insoluble in too dilute sodium hydroxide it dissolves in 2% alkali with a cherry-red color It gives a deep orange-brown solution in conc. sulfuric acid.

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[1] Mathëus, *Ber.*, 21, 1642 (1888).

Subs, 0.1364 15.3 cc N (19.0°, 754 mm)
Calc for $C_{25}H_{28}O_2N_4$ N, 13.46 Found 13.02

Phenylazo-hydrocupreine Dihydrochloride.—The purified base was dissolved in a small volume of 10% hydrochloric acid, chilled, and seeded with crystals obtained by dissolving a test portion in 1 : 1 hydrochloric acid and adding saturated salt solution. After standing in the ice box, the salt was recrystallized from a small volume of 10% hydrochloric acid and let stand at 0°, separating as dark red, felted needles containing 4 molecules of water of crystallization When rapidly heated to 180°, then slowly, the anhydrous salt decomposes at 181–3° with preliminary darkening and sintering, and dissolves readily in the cold in water, alcohol, methyl alcohol, or chloroform It is almost insoluble in dry ether or hot benzene and only sparingly soluble in hot dry acetone. An aqueous solution is readily decolorized by stannous chloride with the formation of aniline hydrochloride and the hydrochloride of aminohydrocupreine.

For analysis the salt was dried *in vacuo* first at room temperature over sulfuric acid and crushed alkali and finally at 80° over sulfuric acid.

Subs, air-dry, 0.5910 loss, 0.0768
Calc. for $C_{25}H_{28}O_2N_4.2HCl.4H_2O$ H_2O, 12.84 Found: 12.99
Subs., anhydrous, 0.1325 13.0 cc. N (23.0°, 760 mm) Subs, 0.1038: AgCl, 0.0578.
Calc for $C_{25}H_{28}O_2N_4.2HCl$ N, 11.45, Cl, 14.49 Found N, 11.32, Cl, 13.78

***o*-Tolylazo-hydrocupreine.**—The purified amorphous dye was dissolved in a small volume of hot absolute alcohol, chilled, and seeded with crystals formed by the spontaneous evaporation of an alcoholic solution of a test portion. The dye slowly crystallized as deep red, spherular masses of microscopic crystals which darken and sinter above 100°, melting to a tar from 110 to 130° It is readily soluble in boiling methyl or ethyl alcohol, sparingly at 0°, and dissolves very easily in chloroform or benzene, less readily in dry acetone. It dissolves in conc sulfuric acid with an orange-red color and partially in hot 5% sodium hydroxide, yielding a cherry-red solution. In dilute acids the color is orange-red.

Subs, 0.1413 16.2 cc N (24.0°, 758.5 mm.)
Calc. for $C_{26}H_{30}O_2N_4$ N, 13.02 Found 13.16.

***m*-Tolylazo-hydrocupreine.**—The purified base was obtained in good usual neutral organic solvents, and is quite soluble in cold *N* sodium hydroxide and practically completely, on boiling, forming a dull red solution. It gradually melts above 103° with preliminary sintering, becoming completely fluid at 125–30°.

Subs, 0 1119: 12 6 cc N (27.0°, 765 mm)
Calc for $C_{26}H_{30}O_2N_4$ N, 13 02 Found 12 89.

The Dihydrochloride.—The base was rubbed under sufficient conc. hydrochloric acid to give a reaction strongly acid to congo red paper and the solution diluted with dry acetone. On adding dry ether until a slight permanent turbidity formed the salt gradually separated on standing and rubbing as aggregates of red, microscopic crystals. After air-drying, the salt contained approximately 1 5 molecules of water of crystallization. When anhydrous it darkens and softens above 160° and decomposes at about 195°. It is very easily soluble in dry methyl alcohol, less easily in absolute alcohol. It dissolves with difficulty in dry acetone or chloroform but is quite soluble in the latter on boiling. It is readily soluble in water with a reddish orange color.

Subs, 0 6548: loss, 0 0373 *in vacuo* at room temp over H_2SO_4 + NaOH
Calc for $C_{26}H_{30}O_2N_4$ 2HCl 1 $5H_2O$. H_2O, 5 70 Found 5 09
Subs., anhydrous, 0 1034 10 1 cc N (26.0°, 757 mm) Subs, 0.1442 AgCl, 0 0832.
Calc for $C_{26}H_{30}O_2N_4$ 2HCl N, 11 14, Cl, 14 09 Found N, 11.11, Cl, 14 27

***p*-Tolylazo-hydrocupreine.**—The crude dye was made to crystallize by warming with 85% alcohol, the separation being completed after cooling by the cautious addition of about $^1/_3$ volume of water. Recrystallized from amyl alcohol, in which it dissolves readily at the boiling point and sparingly in the cold, it forms glistening, orange-red leaflets. When rapidly heated to 200°, then slowly, the dye melts at 202–5° with gas evolution and preliminary softening. It is rather sparingly soluble in the cold in absolute methyl or ethyl alcohol or acetone, but quite readily on warming, and also dissolves easily in chloroform or toluene. The solution in conc. sulfuric acid is bright red, and orange-red in dil. acids.

Subs, 0 1511: 17 2 cc. (N 26.5°, 752 mm)
Calc for $C_{26}H_{30}O_2N_4$: N, 13.02. Found, 12.84

α-Naphthylazo-hydrocupreine.—On dissolving the purified dye in dry acetone it separated almost immediately as glistening, copper-colored, diamond-shaped platelets. It separates from alcohol as deep maroon plates with a bronzy luster, which crush to a dark, purplish red powder and melt slowly to a tar at 146–9° with preliminary sintering. It is soluble in hot alcohol or acetone, more so in the cold in methyl alcohol or benzene, very readily in chloroform, and only sparingly in dry ether and in hot dil. sodium hydroxide. It yields a bright red solution in dil. hydrochloric acid and a deep blue color in conc. sulfuric acid

Subs., 0.1232: 13.0 cc. N (20 5°, 756 mm.).
Calc. for $C_{29}H_{30}O_2N_4$: N, 12 02. Found: 12.21.

β-Naphthylazo-hydrocupreine.—In the purification of the crude dye it was found necessary to use warm dil. hydrochloric acid, as the hydrochloride tended to separate from cold solutions in gelatinous form. Recrystallized from amyl alcohol, in which it is soluble only near the boiling point, the base separates as glistening, woolly, scarlet needles which decompose at 240–4°. The solution in dil. hydrochloric acid is bright orange-red, while that in sulfuric acid is deep violet. It is soluble in chloroform but only very difficultly soluble in alcohol, dry acetone or benzene, and is insoluble in hot dil. sodium hydroxide solution.

Subs., 0.1037: 11 0 cc. N (21 5°, 754 mm.).
Calc. for $C_{29}H_{30}O_2N_4$. N, 12.02. Found: 12 20.

Diphenyl-*p*-bisazo-hydrocupreine.—1.4 g. of benzidine were dissolved in hot water containing 13 g. of conc. hydrochloric acid, chilled, and diazotized with 1.05 g. of sodium nitrite. The solution was coupled with 4.5 g. of hydrocupreine dissolved in 180 cc. of *N* sodium hydroxide diluted to 300 cc. The resulting dye was purified in the usual manner, yielding 4.5 g. of an amorphous product. When dissolved in pyridine, filtered, and cautiously treated with water the dye precipitated as a dubiously crystalline, purplish brown powder. It melts to a tar, with preliminary sintering, above 204° and decomposes at about 220°. The dye is easily soluble in chloroform, sparingly in absolute alcohol or benzene, and very difficultly in dry ether. It dissolves in dil. acids with a deep, purplish red color and only partially in boiling *N* sodium hydroxide solution with a dull red color. The solution in conc. sulfuric acid is an intense violet-blue.

Subs., 0.1178: 13 3 cc. N (28.0°, 758 mm.).
Calc. for $C_{50}H_{54}O_4N_8$: N, 13.49. Found 12.77.

***m*-Nitrophenylazo-hydrocupreine.**—Modification of the usual procedure was necessary in this case, as otherwise the yield was very poor. 2.1 g. of *m*-nitraniline were dissolved by heating with 12.7 g. of conc. hydrochloric acid and about an equal volume of water, rapidly chilled to form a paste of small crystals of the hydrochloride, and diazotized below 10° with a conc. sodium nitrite solution. A solution of 4.5 g. of hydrocupreine was prepared with 200 cc. of *N* sodium hydroxide, diluting to 300 cc. and cautiously adding 14.3 g. of sodium bicarbonate (enough to combine with all but 2 equivalents of the free alkali), stirring until clear, and chilling to 10–15°. After slowly adding the diazo solution and stirring for 15 minutes, the orange dye was filtered off and purified in the usual way, a relatively large amount of acid-insoluble by-products remaining on the filter. The purified product was dissolved in boiling alcohol and separated on cooling and rubbing. Recrystallized from alcohol it forms aggregates of red platelets with an orange luster, which melt at 150.5–

1.5° to a turbid liquid and yield an orange-red powder when crushed. It dissolves in conc. sulfuric acid or in dil. acids with a red-orange color and gives a deep red solution in boiling N sodium hydroxide. It is quite readily soluble in boiling absolute methyl or ethyl alcohol, somewhat sparingly in the cold, but dissolves more easily in cold acetone, benzene, or chloroform.

Subs., 0.1164: 15.3 cc. N (26.0°, 762 mm.).
Calc. for $C_{25}H_{27}O_4N_5$: N, 15.19. Found: 15.05.

***p*-Nitrophenylazo-hydrocupreine.**—A diazotized *p*-nitraniline solution was slowly added to a solution of hydrocupreine prepared in exactly the same way as in the preceding case. The brown-orange precipitate of the dye was washed with water, sucked as dry as possible, and added to boiling alcohol, a portion beginning to crystallize even from the boiling solution. Recrystallized from butyl alcohol it forms brown-red. glistening plates and flat prisms which appear orange under the microscope and crush to an orange-red powder. The substance gradually darkens and softens above 200° and melts and decomposes at about 220°. It dissolves in conc. sulfuric acid or in dil. acids with a red-orange color and gives a deep purple solution in boiling N sodium hydroxide. It is rather sparingly soluble even in boiling absolute alcohol or dry acetone, somewhat more easily in boiling methyl alcohol, and is quite soluble in boiling benzene, difficultly in the cold. Cold chloroform dissolves it very readily.

Subs., 0.1218: 16.3 cc. N (25.5°, 761 mm.).
Calc. for $C_{25}H_{27}O_4N_5$: N, 15.19. Found: 15.32.

***m*-Acetaminophenylazo-hydrocupreine.**—In the case of *m*-amino acetanilide hydrochloride[1] after coupling was complete the dye was thrown out from the deep purple solution by the addition of ammonium chloride. As it showed a tendency to run through the filter when washed with water, a little ammonia was added to the wash water, inhibiting this tendency. The purified substance forms a deep maroon, amorphous powder with a greenish reflex which slowly melts from 155 to 180° after preliminary darkening and sintering. It gives a brown solution in conc. sulfuric acid appearing red-brown by transmitted light, and a deep red color in dil. hydrochloric acid. It melts under dry methyl or ethyl alcohol and dissolves partially, forming deep red solutions. It is rather sparingly soluble in dry acetone but dissolves readily in chloroform. The color in dil. sodium hydroxide solution is a deep purplish red.

Subs., 0.1048: 13.8 cc. N (25.0°, 758 mm.).
Calc. for $C_{27}H_{31}O_3N_5$: N, 14.80. Found: 15.04.

***m* - Uraminophenylazo - hydrocupreine.**—*m*-Aminophenylurea hydrochloride[2] coupled almost at once, forming a deep purple solution from which the dye was precipitated with ammonium chloride as orange flocks which tended to form a colloidal solution on washing with water. Addition of a few drops of ammonia to the wash water diminished this tendency. The purified dye forms an amorphous powder which darkens and sinters above 140° and gradually melts, swells, and decomposes at 165–85°. It dissolves in dil. hydrochloric acid with an orange-red color and in dil. alkali giving a cherry-red solution. The solution in conc. sulfuric acid is a deep brown-orange. The dye melts under dry methyl or ethyl alcohol and then dissolves, more easily in the former It is less soluble in dry acetone or chloroform and only very slightly in boiling water.

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[1] THIS JOURNAL, 39, 1448 (1917).

[2] *Ibid.*, 39, 1449 (1917).

Subs., 0 1077: 17.2 cc N (25.0°, 753 mm).
Calc. for $C_{26}H_{30}O_3N_6$: N, 17.72. Found: 18.13.

***p*-Aminophenylazo-hydrocupreine.**—The acetamino compound (see below) was boiled for one hour with 5 parts of 1 : 1 hydrochloric acid and the solution diluted, filtered, and made alkaline with ammonia. Reprecipitated with ammonia from its solution in very dil. hydrochloric acid, it separates as purplish brown, amorphous flocks which melt at 155–65° with preliminary softening. It is slightly soluble in cold water with a purplish color, more easily in boiling water with a brownish red color, and yields an orange-brown solution in conc. sulfuric acid. An aqueous suspension dissolves with a deep red color on adding a drop of acetic acid, changing to orange-brown with excess of hydrochloric acid. It dissolves readily in methyl or ethyl alcohol, acetone, or chloroform, less easily in cold benzene.

Subs., 0.1152: 15.6 cc. N (22.5°, 765 mm.).
Calc. for $C_{25}H_{29}O_2N_5$: N, 16.24. Found: 15.75.

***p*-Acetaminophenylazo-hydrocupreine.**—Precipitation of the dark red dye was completed by the addition of ammonium chloride. On diluting a methyl alcoholic solution of the purified, amorphous substance with water until the initial turbidity just redissolved, and seeding with crystals deposited on spontaneous evaporation of a test portion in methyl alcohol, the substance crystallized slowly as deep maroon, glistening, microscopic rhombs containing 1.5 molecules of water of crystallization, the separation being completed by the cautious addition from day to day of small amounts of hot water. The anhydrous substance melts to a tar at 158–62° with preliminary softening. It dissolves readily in methyl or ethyl alcohol, or acetone, less easily in benzene. In dil. sodium hydroxide it forms a purple-red solution and dissolves in conc. sulfuric acid with an orange-red color.

Subs., air-dry, 0.3677: Loss, 0.0201 *in vacuo* at 80° over H_2SO_4.
Calc. for $C_{27}H_{31}O_3N_5.1.5H_2O$: H_2O, 5.40. Found: 5.47.
Subs., anhydrous, 0.1308: 17.4 cc. N (25.5°, 747 mm.).
Calc. for $C_{27}H_{31}O_3N_5$: N, 14.80. Found; 14.95.

***p*-Uraminophenylazo-hydrocupreine.**—The purified dye from *p*-aminophenylurea[1] was dissolved in a rather large volume of 85% alcohol and cautiously diluted with water until the turbidity just redissolved. On standing and rubbing crystallization slowly started and was aided from time to time by the careful addition of water. The substance formed deep maroon, rhombic crystals accompanied by small amounts of amorphous material, but the amount obtained was too small for further purification. The anhydrous substance blackens and sinters above 170° and swells and chars at about 190°. It melts under absolute methyl or ethyl alcohol and dissolves partially, but is not very soluble even on boiling. It is sparingly soluble in hot, dry acetone or chloroform, and dissolves in conc. sulfuric acid with a deep red color. The solution in dil. alkali is purplish red and red in dil. acid.

Subs., 0.1276. 20.2 cc. N (26.0°, 756 mm.).

Calc. for $C_{26}H_{30}O_3N_6$ N, 17.72 Found: 17.99.

***p* - Hydroxyphenylazo - hydrocupreine.**—*p* - Benzoyloxy-phenylazo-hydrocupreine dihydrochloride (see below) was dissolved in hot 95% alcohol and the solution chilled and treated with 25% sodium hydroxide solution, causing precipitation of a portion of the dye as a gum. This was redissolved in hot 95% alcohol, added to the main portion, and the whole made strongly alkaline with 25% sodium hydroxide. After about 10 minutes the dark, cherry-red solution was poured into water and treated with an excess of saturated ammonium chloride solution, precipitating the hydroxy dye, which was filtered off and dried. When starting with the quantities given below, the yield was 4.0 g. The crude dye was powdered and boiled with dry acetone, crystallizing before all was dissolved. After chilling and washing with a little cold, dry acetone the substance was recrystallized by dissolving in hot commercial butyl alcohol, cooling, adding an equal volume of dry ether, and then ligroin to incipient turbidity, filtering, seeding, and letting stand in the ice box. The dye separated as spherules of deep maroon, microscopic needles which may be pulverized to a dark brown-red powder and retain $^1/_2$ molecule of butyl alcohol of crystallization on drying *in vacuo* over calcium chloride and paraffin, the solvent being given off very slowly even at 100° *in vacuo* over sulfuric acid. The solvent-free substance gradually melts, blackens and swells at 150–60° and is readily soluble in dry methyl or ethyl alcohol with a brown-red color. It is less soluble in cold dry acetone, dissolving on boiling with a bright red color. It gives an intense red color in conc. sulfuric acid, appearing purplish in thin layers, and dissolves in dil. hydrochloric acid with a bright red, in dil. sodium hydroxide with a cherry-red color. A solution in warm 10% hydrochloric acid deposits the dihydrochloride on cooling as delicate, red needles.

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[1] This Journal, 39, 1456 (1917).

Subs., dried at room temp., 0.3740: loss, 0.0304 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{25}H_{28}O_3N_4.0.5C_4H_9OH$: 7.89. Found 8.13.
Subs., solvent-free, 0.1265: 14.2 cc. N (24.0°, 761 mm.)
Calc. for $C_{25}H_{28}O_3N_4$: N, 12.96. Found, 12.92

***p*-Benzoyloxy-phenylazo-hydrocupreine dihydrochloride.**—3.6 g. of *p*-aminophenyl benzoate were diazotized by suspending in a little water, adding 5.5 g. of conc. hydrochloric acid, and very slowly dropping in 3.3 cc. of 5 *N* sodium nitrite solution. The filtrate was slowly added to a solution of 4.7 g. of hydrocupreine in 120 cc. of *N* aqueous sodium hydroxide, to which 50 cc. of water and 7.7 g. of sodium bicarbonate (leaving 2 mols. of uncombined alkali) had been added with vigorous stirring. The dye, which separated rapidly, was filtered off, dissolved in dil. hydrochloric acid, the solution filtered, and treated with saturated salt solution until the initial turbidity just redissolved. On seeding with crystals obtained by precipitating a portion of the solution with sodium chloride and letting stand, the dihydrochloride separated rapidly and was washed with 10% hydrochloric acid, dissolved in 50% alcohol, and treated with an equal volume of the 10% acid. On seeding and chilling the dihydrochloride separated as minute, orange needles containing 2.5 molecules of water of crystallization and dissolving quite freely in water with a red-orange color, leaving a trace of insoluble material. The anhydrous salt melts, blackens, and decomposes at about 185–95°, and dissolves readily in cold dry methyl alcohol, less easily in absolute alcohol. It is sparingly soluble in boiling dry acetone, more easily in dry chloroform. It dissolves in conc. sulfuric acid with an intense red color, appearing purplish in thin layers, the same colors being observed in the clear solution obtained by diluting an alcoholic solution with *N* aqueous sodium hydroxide.

Subs., air-dry, 0.6640: loss, 0.0483 *in vacuo* at room temp. over H_2SO_4 + NaOH.
Calc. for $C_{32}H_{32}O_4N_4.2HCl.2.5H_2O$: H_2O, 6.89. Found 7.27
Subs., anhydrous, 0.1239: 10.0 cc. N (28.0°, 759 mm.) Subs., 0.2259: AgCl, 0.0998.
Calc. for $C_{32}H_{32}O_4N_4.2HCl$: N, 9.20; Cl, 11.63. Found: N, 9.14; Cl, 10.93.

2-Methoxyphenylazo-hydrocupreine.—During the coupling the scarlet dye separated almost immediately. The purified substance forms a dark red, amorphous powder which darkens and softens above 105°, melts to a tar above 120° and is completely fluid at about 160°. It is easily soluble in alcohol, acetone or benzene, less readily in ether. It dissolves in conc. sulfuric acid with an intense purplish red color and in dil. acids with a redder shade than the phenyl or tolyl compounds. It is soluble in hot 5% sodium hydroxide solution with a cherry-red color.

Subs., 0.1076: 12.4 cc. N (30.0°, 752 mm.).
Calc. for $C_{26}H_{30}O_3N_4$: N, 12.55. Found: 12.85.

3-Methoxyphenylazo-hydrocupreine

m-anisidine[1] was dried and ground in a mortar with about 25 cc. of commercial butyl alcohol. The substance dissolved and then quickly crystallized out in a yield of 3.9 g. Recrystallized from butyl alcohol it separates as dark red rhombs with a golden luster, crushing to an orange-red powder and melting at 188–90°, with slight gas evolution and preliminary softening. It dissolves only partially in boiling *N* sodium hydroxide solution, but if dissolved in a little alcohol and then diluted with *N* sodium hydroxide a clear, deep cherry-red solution is obtained. The dye dissolves in dil. acids with an orange-red color and in conc. sulfuric acid with a deep brown-red color. It dissolves readily in cold chloroform and rather sparingly in cold benzene but readily on boiling. It is difficultly soluble in cold dry methyl or ethyl alcohol, or dry acetone, somewhat more easily on boiling.

Subs., 0.1202: 13.2 cc. N (24.0°, 763 mm.).
Calc. for $C_{26}H_{30}O_3N_4$: N, 12.55. Found: 12.68.

4-Methoxyphenylazo-hydrocupreine.—The crude, washed dye was warmed with 85% alcohol, rapidly changing to the crystalline form. Recrystallized from amyl alcohol it forms deep red, glistening plates which decompose with gas evolution above 207°, sintering to a tar, and finally melting at 213–5° with further gas evolution. It dissolves more freely in chloroform than in the other usual solvents, and is readily soluble in hot benzene or amyl alcohol, sparingly in the cold. It yields a bright red solution in dilute acids and dissolves in conc. sulfuric acid with a deep purple color, changing to deep red, with a purple fluorescence.

Subs., 0.1409: 15.0 cc. N (21.0°, 754 mm.).
Calc. for $C_{26}H_{30}O_3N_4$: N, 12.55. Found: 12.27.

2-Ethoxyphenylazo-hydrocupreine.—The yield of the purified dye was equal to the hydrocupreine used. It forms a scarlet, amorphous powder, less easily soluble in ligroin than in the other usual neutral organic solvents. It softens at about 100°, melts gradually above 110°, and is completely fluid at 135–40°. It dissolves in dil. hydrochloric acid with a bright red color and is slightly soluble in cold *N* sodium hydroxide solution, more easily on boiling. The solution of the dye in conc. sulfuric acid is deep reddish purple by reflected light and purplish red by transmitted light.

Subs., 0.1146: 12.5 cc. N (31.0°, 758 mm.).
Calc. for $C_{27}H_{32}O_3N_4$: N, 12.17. Found: 12.22.

3-Ethoxyphenylazo-hydrocupreine.—The yield of the purified dye was slightly less than the amount of alkaloid used. It forms an orange-red powder which is less easily soluble in ligroin or ether than in the other usual neutral organic solvents. It is partly soluble in the cold in *N* sodium hydroxide solution and dissolves in dil. hydrochloric acid with a deep orange-red color. It gives a deep, brown-red color in conc. sulfuric acid. The substance sinters and darkens above 75°, melts slowly above 90°, and is completely fluid at about 125°.

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[1] This Journal, 41, 1452 (1919).

Subs., 0.1113: 11.7 cc. N (27.0°, 758 mm.).
Calc. for $C_{27}H_{32}O_3N_4$: N, 12.17. Found: 11.93.

4-Ethoxyphenylazo-hydrocupreine.—A ligroin solution of the purified, amorphous dye deposited the compound on standing as microscopic rhombs. However, the dye may be obtained as large, almost black rhombs by dissolving in hot 85% alcohol, cooling to 0°, diluting very cautiously with water until the initial turbidity just redissolves, seeding, and letting stand in the ice box. The crystals weathered in the air, probably owing to loss of water of crystallization. The pulverized crystals form a bright red powder, and, when anhydrous, darken and soften above 100° and melt at 156–61° when the bath is slowly heated. The substance melts when plunged into the bath at 130°. It dissolves in dil. hydrochloric acid with a bright red color, and is soluble with a purplish red color in hot, dil. sodium hydroxide solution. It dissolves quite easily in the usual neutral organic solvents with the exception of ligroin. The deep red solution in conc. sulfuric acid appears purple in thin layers and fluoresces purple.

Subs., 0.1369: 14.3 cc. N (21.5°, 755 mm.).
Calc. for $C_{27}H_{32}O_3N_4$: N, 12.17. Found: 12.03.

3,4-Methylenedioxy-phenylazo-hydrocupreine.—The dried, purified dye was dissolved in hot, dry acetone and the cooled solution filtered from a little insoluble matter and seeded with crystals obtained by allowing a test portion to stand in 70% alcohol. The substance separated on standing, the process being made more complete by the addition of small portions of water from time to time. As obtained in this way it forms deep maroon, apparently microcrystalline crusts which melt at 177–84° with slow gas evolution and slight preliminary darkening and softening. It dissolves in conc. sulfuric acid with an intense blue color and in dil. acids with a deep red shade. A suspension in boiling *N* sodium hydroxide solution dissolves only incompletely, but on diluting an alcoholic solution with *N* sodium hydroxide a clear, deep red solution is obtained. It dissolves easily in cold chloroform, less readily in the cold in dry methyl or ethyl alcohol, dry acetone, or benzene, but more freely on boiling.

Subs., 0.1255: 13.1 cc. N (24.5°, 763 mm.).
Calc. for $C_{26}H_{28}O_4N_4$: N, 12.17. Found: 12.02.

3,4-Dimethoxy-phenylazo-hydrocupreine.—Analysis showed that the usual purification process was insufficient. The dye was accordingly dissolved in acetone and treated with ligroin until about 10% had been precipitated as dark flocks. The mixture was filtered and the filtrate shaken out with water. The ligroin layer, from which most of the dye had separated, clinging to the walls of the separatory funnel, was shaken out with dil. hydrochloric acid and the solution filtered, diluted to large volume, and the dye precipitated with dil. ammonia. It forms a red, amorphous powder, which darkens above 90°, begins to melt at about 110°, and is completely fluid at about 180°. It dissolves in dil. acids with a bright red color, in dil. alkali with a cherry-red color, and is readily soluble in the usual neutral organic solvents with the exception of ligroin. The solution in conc. sulfuric acid is an intense red-violet in thick layers, and blue-violet in thin layers.

Subs., 0.1028· 10 8 cc. N (30 0°, 755)
Calc. for $C_{27}H_{32}O_4N_4$: N, 11.76. Found: 11.77.

3-Methoxy-4-ethoxyphenylazo-hydrocupreine.—Purification of the dye (from hydrocupreine and diazotized 3-methoxy-4-ethoxyaniline[1]) by the usual process failed to yield a pure product, so the dye was dissolved in a small volume of dry acetone and freed from a dark, flocculent impurity exactly as in the case of the dimethoxy compound. It forms a deep red powder which begins to darken and soften at about 80°, gradually melts above 100°, and is completely fluid at about 135°. It dissolves readily in the usual neutral organic solvents except ligroin, and is soluble in dil. sodium hydroxide with a cherry-red color and in dil. acids with a deep red color. The solution in conc. sulfuric acid is an intense violet, appearing blue in thin layers.

Subs, 0.1003. 9.8 cc. N (21 5°, 766 mm).
Calc. for $C_{28}H_{34}O_4N_4$. N, 11 43. Found. 11 41.

4 - Methoxy - 5 - ethoxyphenylazo - hydrocupreine.—4 - Methoxy - 5 - ethoxyaniline[2] was diazotized, coupled with hydrocupreine, and the product purified exactly as in the case of its 3,4-isomer. The yield of dark red, amorphous product was 80% of the alkaloid taken. It was not entirely soluble in dil. sodium hydroxide solution and dissolved in dil. acids with a deep red color. It is less easily soluble in ligroin or ether than in the other usual neutral organic solvents. The dye dissolves in conc. sulfuric acid with an intense violet color, appearing redder by transmitted light than by reflected light. It softens and gradually melts above 75°, becoming completely fluid at about 120°.

Subs, 0.1308: 12.6 cc N (23 5°, 769 mm.).
Calc. for $C_{28}H_{34}O_4N_4$· N, 11.43. Found: 11.23.

3,4 - Dimethoxy - 6 - carboxyphenylazo - hydrocupreine.—After coupling 6-aminoveratric acid[3] with hydrocupreine in the usual way the deep red solution was treated with ammonium chloride, precipitating the dye (not the salt in this case) as a brick-red amorphous precipitate. This was purified with the aid of dil. hydrochloric acid and the filtrate treated with sodium acetate solution. The dye forms a deep maroon powder which, when rapidly heated to 235°, then slowly, melts and decomposes at 236°. It is rather difficultly soluble in the usual solvents and dissolves in dil. hydrochloric acid with a cherry-red color and in dil. sodium hydroxide with a somewhat brighter red shade. The color in conc. sulfuric acid is an intense violet.

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[1] THIS JOURNAL, 41, 1461 (1919).

[2] *Ibid.*, 41, 1462 (1919).

[3] This substance, which does not seem to have been previously described, was prepared by nitrating methyl veratrate in acetic acid solution with fuming nitric acid, reducing to the amino ester (cf. Zincke and Francke, *Ann.*, 293, 190 (1896)) with a solution of stannous chloride in methyl alcoholic hydrochloric acid, diluting with ice and

Subs., 0.1224. 11 4 cc N (27 0°, 757 mm)
Calc. for $C_{18}H_{22}O_4N_4$ N, 10 77 Found 10 56

O - **Phenylglycollic acid - *p* - azohydrocupreine,** *p* - $HO_2C.H_2C.O.C_6H_4N : NC_{19}H_{23}O_2N_2$.—The deep purplish red solution obtained on coupling *p*-aminophenoxyacetic acid[1] was acidified with a slight excess of acetic acid and the deep red precipitate filtered off and heated with 85% alcohol. The substance began to crystallize but dissolved entirely on adding sufficient boiling 85% alcohol. The solution was diluted with about $^1/_2$ volume of water, treated with a few drops of acetic acid, and seeded, and the product recrystallized from 50% alcohol, separating rapidly on seeding the cooled, supersaturated solution as brilliant, red needles containing 4 molecules of water of crystallization. An aqueous suspension dissolves only on adding a considerable excess of acetic acid, but dissolves easily on adding a drop or two of dil. sodium carbonate or hydroxide with a purplish red color, changing to orange-red on addition of hydrochloric acid. When rapidly heated to 195°, then slowly, the anhydrous acid darkens, softens, and sinters, finally melting at 199–200° with decomposition. It dissolves readily in chloroform or acetone, sparingly in dry methyl or ethyl alcohol, and gives a deep red color in conc. sulfuric acid, appearing purple in thin layers.

Subs, air-dry, 0 3940: loss, 0 0496 *in vacuo* at 100° over H_2SO_4
Calc for $C_{27}H_{30}O_5N_4.4H_2O$ H_2O, 12 82 Found 12 58.
Subs, anhydrous, 0 1235: 12 6 cc N (23 5°, 752 mm.)
Calc for $C_{27}H_{30}O_5N_4$: N, 11.43. Found 11 62

m - **Carboxamido - phenylazo - hydrocupreine,** *m* - $H_2NOCC_6H_4N$:-

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water, and extracting the amino ester after making alkaline Saponified with alcoholic sodium hydroxide on the water bath and evaporated, this yielded the acid as a mass of needles after diluting with water and acidifying with acetic acid. Recrystallized from ethyl acetate, it forms almost colorless, thick plates which dissolve with difficulty in boiling water and are somewhat more readily soluble in acetone than in the other neutral organic solvents. When rapidly heated to 185°, then slowly, it effervesces at 186°. An aqueous suspension gives an indigo-blue color with ferric chloride.

Subs., 0.1439: 9.2 cc. N (24 0°, 753 mm).
Calc. for $C_9H_{11}O_4N$: N, 7.11. Found: 7.07.

[1] THIS JOURNAL, 39, 2196 (1917).

$NC_{19}H_{22}O_2N_2$.—The dye from *m*-aminobenzamide[1] was purified in the usual way, forming an amorphous powder which sinters and darkens above 135°, begins to melt at 160°, and is completely fluid and decomposes at about 195°. It dissolves readily in alcohol, less easily in dry chloroform or acetone, or benzene, and dissolves in *N* sodium hydroxide solution with a deep cherry-red color.

Subs, 0 1077 14 2 cc N (24 0°, 757 mm)
Calc for $C_{26}H_{29}O_3N_5$ N, 15 25 Found 15 09

On rubbing the base with 1 1 hydrochloric acid it dissolves and the solution soon deposits the *dihydrochloride* as aggregates of flat, orange-red, microscopic needles

***p*-Sulfophenylazo-hydrocupreine.**—Sulfanilic acid coupled practically instantaneously with hydrocupreine under the usual conditions. Saturated ammonium chloride solution was added at the end in order to free the hydroxyl group. The scarlet *sodium salt* precipitated immediately, the amount increasing slightly on addition of sodium chloride. After washing with saturated sodium chloride solution a portion was recrystallized from water, separating on gradual cooling as glistening, scarlet rhombs and prisms which soon lose a portion of their water of crystallization on air-drying, turning a darker red and coming to equilibrium with 3.5 molecules of water of crystallization The salt dissolves in water with a deep brown red color, changing to cherry-red on adding alkali Dilute aqueous solutions give slow-forming, red rhombs of the calcium and barium salts.

Subs air-dry, 0 5788 loss, 0 0618 *in vacuo* at 80° over H_2SO_4
Calc for $C_{25}H_{27}O_5N_4SNa$ 3 $5H_2O$ H_2O, 10 85 Found 10 68
Subs, anhydrous, 0 1213 11 2 cc N (24 5°, 764 mm)
Calc for $C_{25}H_{27}O_5N_4SNa$ N, 10 81 Found 10 65

A portion of the crude salt was dissolved in much hot water and acidified slightly with acetic acid, the *free sulfonic acid* soon separating as brilliant, brown-orange leaflets Recrystallized from 50% alcohol it separates slowly as gleaming, red prisms containing 3 molecules of water of crystallization and dissolving with difficulty in boiling water. The anhydrous acid, when rapidly heated to 250°, then slowly ,melts and decomposes at 252° with preliminary darkening and softening It dissolves in sulfuric acid with a red-orange color, and is appreciably soluble in dry methyl alcohol, less readily in absolute alcohol or dry chloroform. An aqueous suspension dissolves readily in dil. mineral acids, but only on adding a large excess of acetic acid.

Subs, air-dry, 0 5158 loss, 0 0500 *in vacuo* at 100° over H_2SO_4
Calc for $C_{25}H_{28}O_5N_4S$ $3H_2O$: H_2O, 9 82 Found: 9 70
Subs, anhydrous, 0 1293. 12 6 cc. N (26.0°, 762 mm.).
Calc. for $C_{25}H_{28}O_5N_4S$: N, 11 29. Found: 11.16.

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[1] THIS JOURNAL, 39, 1438 (1917).

m - Sulfonamido - phenylazo - hydrocupreine, *m* - $H_2NO_2SC_6H_4N$:-$NC_{19}H_{23}O_2N_2$.—As obtained by the ordinary process of purification the dye from *m*-aminobenzene-sulfonamide[1] was still impure and it was accordingly dissolved in acetone and fractionally precipitated with ligroin, rejecting the first portions. The last fractions were dissolved in dil. hydrochloric acid and reprecipitated with ammonia, but the percentage of nitrogen was still low. The orange-brown, amorphous dye softens and sinters above 140°, gradually melts above 170°, and is completely fluid at about 190°. It dissolves in conc. sulfuric acid with an orange-red color, in dil acids with an orange color, and in dil. sodium hydroxide with a deep cherry-red color.

Subs., 0 1018 12 2 cc N (30 5°, 757 mm).
Calc for $C_{25}H_{29}O_4N_5S$: N, 14.13. Found: 13 43.

***p*-Sulfonamido-phenylazo-hydrocupreine.**—The dye obtained from *p*-aminobenzene-sulfonamide[2] was purified in the usual way. It forms an orange-brown amorphous powder which gradually melts above 155° and is completely fluid at about 190°. It dissolves in conc. sulfuric acid with a brown-orange color, in dil. acids with a red-orange color, and gives a deep cherry-red solution in dil. sodium hydroxide. It is readily soluble in alcohol, sparingly in benzene.

Subs, 0 1321: 15 7 cc. N (21 0°, 750 mm).
Calc. for $C_{25}H_{29}O_4N_5S$ N, 14.13 Found: 13 62.

Quinolyl-6-azohydrocupreine.—The crude dye from 6-aminoquinoline crystallized suddenly when warmed with 85% alcohol. Recrystallized from amyl alcohol it separated slowly as aggregates of bright red, glistening, lenticular platelets with a golden reflex. When rapidly heated to 230°, then slowly, the substance melts and evolves gas at 232–4°, with preliminary softening and darkening. It dissolves readily in chloroform or boiling amyl alcohol, and is rather sparingly soluble in boiling alcohol, acetone, or benzene. An aqueous suspension does not dissolve on adding dil. sodium hydroxide, but an alcoholic solution, diluted with *N* sodium hydroxide, gives a clear, cherry-red solution. The solution in conc. sulfuric acid is reddish orange, while the color in dil. acids is orange-red.

Subs., 0.1342: 17.1 cc. N (22.5°, 752 mm.).
Calc. for $C_{28}H_{29}O_2N_5$: N, 14.98. Found: 14.57.

(B) Azo Dyes Derived from Hydrocupreidine.

Phenylazo-hydrocupreidine.—13 g. of hydrocupreidine[3] were coupled with diazotized aniline in the usual way, completing the precipitation of the dye with ammonium chloride, and purifying by solution in very dilute hydrochloric acid and reprecipitation with ammonia. The yield was 13.9

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[1] This Journal, 39, 2428 (1917).

[2] *Ibid.*, 39, 2429 (1917).

[3] *Ibid.*, 41, 827 (1919).

g. When the amorphous product is dissolved in hot acetone it soon begins to crystallize and a portion for analysis was filtered from the hot solution, as the fractions deposited on cooling were accompanied by a little amorphous material. Recrystallized from alcohol it separates slowly on seeding as a hard crust of garnet-like rhombs which melt at 183–5° with slight preliminary darkening and softening. The substance forms a scarlet powder when crushed, and is appreciably soluble at room temperature in alcohol, methyl, ethyl, or amyl alcohol, or acetone, more easily on boiling. It dissolves readily in chloroform or benzene, and gives a reddish orange-brown color in conc. sulfuric acid.

Subs., 0.1110: 12.4 cc N (22.5°, 772 mm.)
Calc. for $C_{25}H_{28}O_2N_4$: N, 13.46. Found: 13.11.

The Dihydrochloride.—When the amorphous, purified base is dissolved in not too little dry acetone and treated with an excess of conc. hydrochloric acid the dihydrochloride is obtained as an amorphous precipitate which crystallizes almost immediately. The salt was filtered off, moistened with 1 : 1 hydrochloric acid, and treated with dry acetone, filtering again and washing the orange-red platelets with dry acetone containing a drop of conc. hydrochloric acid. The air-dry salt contains 4 molecules of water of crystallization and is readily soluble in water. After drying *in vacuo* at room temperature over sulfuric acid and crushed alkali it turns a bright red, and, when rapidly heated to 215°, then slowly, decomposes at 220–1°, with slight preliminary darkening. It is readily soluble in dry methyl alcohol, less easily in cold chloroform, and dissolves with difficulty in cold absolute alcohol, more readily on warming.

Subs., air-dry, 0.6078: loss, 0.0788.
Calc. for $C_{25}H_{28}O_2N_4.2HCl.4H_2O$: H_2O, 12.84. Found: 12.97.
Subs., anhydrous, 0.1332: 13.2 cc N (22.0°, 760 mm.). Subs., 0.1841: AgCl, 0.1074.
Calc. for $C_{25}H_{28}O_2N_4.2HCl$: N, 11.45; Cl, 14.49. Found: N, 11.48; Cl, 14.43.

α-Naphthylazo-hydrocupreidine.—The purified dye was recrystallized first from alcohol, then from a small volume of amyl alcohol, separating as tufts of deep red, hair-like needles which melt at 132–40° with preliminary darkening, softening, and sintering. It dissolves very easily in chloroform or benzene, somewhat less readily in dry acetone, and sparingly in cold methyl or ethyl alcohol, more easily on boiling. It dissolves in conc. sulfuric acid with a deep blue color, in dilute acids with a red shade, and gives a dull red color in dil. alkali.

Subs., 0.1220: 13.0 cc N (23.5°, 761 mm.).
Calc. for $C_{29}H_{30}O_2N_4$: N, 12.02. Found: N, 12.28.

***p*-Nitrophenylazo-hydrocupreidine.**—Hydrocupreidine and diazotized *p*-nitraniline were coupled exactly as in the case of hydrocupreine (see p. 2136). The crude dye was purified in the usual manner and then crystallized readily when dissolved in boiling alcohol and allowed to cool.

Recrystallized from alcohol it separates on seeding, after cooling and filtering from a small amount of an amorphous impurity, as spherules of red microcrystals which melt to a tar at 135-9° and become completely fluid at 155-60°. It dissolves appreciably in cold methyl or ethyl alcohol, quite readily on boiling, and is very easily soluble in cold chloroform, acetone, or benzene. It dissolves in conc. sulfuric acid or dil. acids with a red-orange color, and in hot dil. *N* sodium hydroxide with a deep purplish red color. An alcoholic solution also gives a clear, deep purple solution when diluted with *N* sodium hydroxide.

Subs., 0.1192: 15.65 cc. N (27.5°, 764 mm.).
Calc. for $C_{25}H_{27}O_4N_5$: N, 15.19. Found 15.00.

p-Sulfophenylazo-hydrocupreidine.—This substance was prepared in the same way as its hydrocupreine isomer. As the crude sodium salt showed no tendency to crystallize it was dissolved in enough hot water to give a clear solution and acidified with acetic acid, seeding with crystals obtained by strongly acidifying a conc. test portion with acetic acid. Recrystallized first from water, then from 50% alcohol, the sulfonic acid separates slowly on seeding as minute orange-red crystals containing 5.5 molecules of water of crystallization, and dissolving appreciably in cold water, more easily on heating. The anhydrous substance is a darker red and, when rapidly heated to 245°, then slowly, it decomposes at 247°, with preliminary darkening and softening. It dissolves in conc. sulfuric or dil. acids with an orange color and in dil. sodium carbonate with a brown-red color, becoming more purple on adding sodium hydroxide. It is quite soluble in dry methyl or ethyl alcohol or chloroform and appreciably in cold, dry acetone.

Subs., air-dry, 0.3397: loss, 0.0533 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{25}H_{28}O_5N_4S.5.5H_2O$. H_2O, 16.64. Found: 16.28.
Subs., anhydrous, 0.1204: 11.7 cc. N (24.5°, 762 mm.).
Calc. for $C_{25}H_{28}O_5N_4S$: N, 11.29. Found. 11.18.

(C) Derivative of 6-Hydroxyquinoline.

Phenylazo-6-hydroxyquinoline.—Aniline was coupled as in the case of the phenolic alkaloids with an alkaline solution of 6-hydroxyquinoline. Precipitation of the dye was completed with ammonium chloride and the crude product recrystallized twice from alcohol, separating as minute, narrow, red leaflets which melt at 160-1.5° with slight preliminary softening, crystallizing again on cooling. In its solubilities, color reactions, and dyeing properties it resembles the corresponding hydrocupreine and hydrocupreidine compounds. The substance was first prepared by Mathëus,[1] who, however, gives no melting point.

Subs., 0.1297: 19.2 cc. N (28.5°, 762 mm.).
Calc. for $C_{15}H_{11}ON_3$: N, 16.87. Found: 16.81.

NEW YORK, N. Y.

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[1] *Ber.*, 21, 1642 (1888).

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ROGER ADAMS.

Author Index to Volume XLI, 1919.

Acree, S. F. See Birge, R. T., White, E. C.
Adams, L. H. See Hall, R. E.
Adams, L. H., Williamson, E. D. and Johnston, J. Detn. of the compressibility of solids at high pressures.......... 12
Adams, R. Alkali-insol. phenols.......... 247
Adams, R. and Rindfusz, R. E. Cyclic ethers from o-allyl phenols—methylene coumaranes... 648
Adams, R. and Voorhees, V. Org. chem. reagents (IV) prepn of alkyl iodides.......... 789
Adkins, H. See Evans, W. L.
Adler, L. See MacInnes, D. A.
Armitage, F. P. Chemistry—First Stage (book rev.).......... 130

Baldwin, M. E. See Sherman, H. C.; Thomas, A. W.
Bancroft, G. R. Prepn. and hydrolysis of esters derived from the substituted aliphatic alcs.. 424
Bates, S. J. and Kirschman, H D. Vapor pressures and free energies of the H halides in aq. soln —free energy of formation of HCl.......... 1991
Beal, G. D. and Okey, R. E. Proximate analysis of *Rumex crispus*, and a comparison of its hydroxymethyl-anthraquinones with those from certain other drugs.......... 693
Beegle, F. M See Nelson, J. M.
Bigelow, L. A. Side chain oxidations with $KMnO_4$.......... 1559
Birge, R. T. and Acree, S. F. Quinone-phenolate theory of indicators—spectrophotometric method for measuring the concns of the quinoidal and lactoidal salts and the equil. and affinity consts. of the phenolphthaleins and phenolsulfonephthaleins.......... 1031
Blair, A. J. Chem Analysis of Fe (book rev.).......... 1315
Bock, J. C. Permanent marking of glass vessels.......... 359
Bogert, M. T. and Ehrlich, J. Unique case of a liquid that exhibits a min soly. in an unstable region, 741; synthesis of certain substituted pyrogallol ethers, including a new acetophenetide derived from the ethyl ether of syringic acid.......... 798
Bogert, M T. and Harris, C. P Synthesis of some homologs of the terpenes, derivs. of 1,4-diisopropylcyclohexane.......... 1676
Bogert, M. T. and Marcus, J. K. Synthesis of aminoflavones, of flavone-azo-β-naphthol dyes, and of other flavone derivs.......... 83
Bogert, M. T. and Scatchard, G. Quinazolines (XXXIV) synthesis of certain nitro- and aminobenzoylene ureas and some compds. related thereto.......... 2052
Bohn, R. T. See Kelley, G. L.
Borgstrom, P. See Porter, C. W.
Boyer, S. See Richards, T. W.
Bracewell, R. S. Mol. mechanism of colloidal behavior (III) chem nature of the adsorption of acids and alkalies by the protein mol, 1511, see Tolman, R. C.
Braham, J. M. Some phys. properties of mannite and its aq solns.......... 1707
Bray, W. C., Simpson, M. E. and MacKenzie, A. A. Volumetric detn. of hydroxylamine.... 1363
Brinton, P. H. M.-P. Single deflection method of weighing.......... 1151
Brinton, P. H. M.-P. and James, C. Detn of Ce in the presence of other rare earths by pptn. as ceric iodate.......... 1080
Britton, E. C. See Hale, W. J.
Brooks, A. P. See Tolman, R. C.
Brown, F. E. See Harkins, W. D.
Brown, O. W. and Carrick, L. L. Catalytic prepn. of the amidophenols and the phenylenediamines.......... 436
Browne, A. W., Holmes, M. E. and King, J. S. Behavior of the hydronitrogens and their derivs. in liquid NH_3 (VI) electrolytic nitridation of various anodes in a soln. of NH_4N_3.... 1769
Browne, C. A. Compn. and calorific value of sirups and molasses derived from sugar cane.... 1432
Browning, P. E. See Porter, L. E.
Buckner, G. D. Translocation of the mineral constituents of the jack bean, 282; compn. of the ash of crab grass as affected by the soil in which it is grown.......... 1384
Bunting, E. N. See Schlesinger, H. I.
Burgess, H. A. See Mueller, E. F.
Byers, H. G. and Thing, C. W. Passivity of Co.......... 1902

Cadwell, S. M. and Leavell, G. Detn. of Au, especially in animal tissue.......... 1
Caldwell, M. L. See Sherman, H. C.
Carr, R. H. See Spitzer, G.

Carrick, L. L. See Brown, O. W.
Carson, C. M. Decompn. of $SnCl_4$ by water and by KOH solns.......................... 1969
Cartledge, G. H. Emanation method of detg. Th, 42; see McCoy, H. N.
Carver, E. K. See Richards, T. W.
Chapin, R. M. As_2O_3 as a standard substance in iodimetry................................ 351
Chatterjee, N. R. See Datta, R. L.
Chatterjee, S. C. and Das, A. K. Condensation of 1-phenyl-3-methyl-5-pyrazolone with anhydrides.. 707
Chesnut, V. K. See Power, F. B.
Clark, G. L. Crit. study of the K and Na double salts of $PbCl_4$ as sources of F............ 1477
Clarke, F. W., Thorpe, T. E. and Urbain, G. Rept. of the Intern. Comm. on At. Wts. for 1919–20.. 1881
Clifford, C. W. Liquid NH_3-Na method for halogens in org compds., the formation of cyanide, and method of removing from the soln.. 1051
Cohen, J. B. Org. Chemistry for Advanced Students (book rev.)............................ 2148
Conant, J B. Prepn. of Na *p*-hydroxyphenyl-arsonate 431
Contieri, A. W. See MacInnes, D. A.
Coolidge, A. S. See Forbes, G. S
Copaux, H. Introduction à la Chimie Générale (book rev.).................................... 1877
Cottrell, F. G. Detn. of b. ps. of solns 721
Craig, W. M. See Richards, T. W.
Crossley, M. L. Certain metallic derivs of hydroxy-anthraquinones, 2081; gentian violet—its selective bactericidal action 2083
Curtman, L. J. and Harris, B R Test for tartrates.. 207

Dains, F. B, Greider, H. W and Kidwell, C. H. *Action of NH_3 and amines on the substituted ureas and urethanes (I) carbonyldiurethane* 1004
Dame, P. A. See Hoffman, E J.
Daniels, F. See Richards, T. W.
Das, A. K. See Chatterjee, S. C.
Das, A. K. and Ghosh, B. N. Diketohydrindene (III).. 1221
Daschavsky, P G See Johnson, T B.
Datta, R. L. Halogenation (XVII) (XVIII) (correction).. 1312
Datta, R. L. and Chatterjee, N. R Halogenation (XVIII) direct iodinization by means *of I and HNO_3* 292
Datta, R. L and Mitter, H K. Halogenation (XVII) action of halogens on Grignard reagent and the replacement of halogen atoms by one another, 287, (XIX) replacement of sulfonic groups by Cl and the prepn. of org. chloro-derivs 2028
Datta, R. L and Varma, P S Replacement of sulfonic groups by nitro groups by means of nitrous gases 2039
Davis, L. and Merker, H. M Pepsin (I) chem changes in the purification of pepsin 221
Davis, T. L. Some factors bearing upon 1,6-addition, 1132; see Kohler, E. P.
Davis, W. S. See Kober, P A
Day, J. E. See Evans, W. L.
Dennis, L. M. and Koller, J. P. Selenic acid and Cu selenate.................................. 949
Doane, F. B. See Pratt, D. S.
Dobbin, L. Manganous tartrate and K manganous tartrate.................................... 934
Dolt, M L. Chem. French (book rev.)... 474
Dougherty, R. H. See Tolman, R. C.
Doughty, H. W. Action of CuCl with compds. contg. the trichloromethyl group............ 1129
Dowell, C. T. Action of Cl on hydrazine, hydroxylamine and urea........................... 124
Dull, C. E. Essentials of Modern Chemistry (book rev.)...................................... 1314

Eastlack, H. See Smith, A.
Ehrlich, J. See Bogert, M. T.
Engelbrecht, H. See Kohler, E. P.
Epple, W. F. See Spitzer, G.
Evans, W. L. and Adkins, H. Oxidation of org. compds. with alk. $KMnO_4$.................. 1385
Evans, W. L. and Day, J. E. Oxidation of EtOH by means of $KMnO_4$......................... 1267
Ewing, D. T. See Harkins, W. D.

Fales, H. A. Conditions affecting the precise detn. of Zn as the sulfide..................... 992
Fales, H. A. and Ware, G. M. Conditions affecting the precise detn. of Zn as the sulfide.... 487
Fall, P. H. See Holmes, H. N.
Fay, H. Advanced Course in Quant. Analysis (book rev.)....................................... 1472

Felsing, W. A. See Keyes, F. G.
Ferguson, J. B. Thermal dissoc of SO_3 69
Fogg, H. C. and James, C. Extn. of Ga and Ge from zinc oxide 947
Forbes, G. S. and Coolidge, A. S Relations between distribution ratio temp. and concn. in system: water–ether–succinic acid 150, 1721

Gerke, R. H. See Tolman, R. C., Wells, P. V.
Ghosh, B. N. See Das, A. K.
Gilman, H. See Kohler, E. P.
Giua, M. Chimica delle sostanze esplosive (book rev.) 1878
Gomberg, M. Ethylene chlorohydrin and β,β'-dichloroethyl sulfide 1414
Gomberg, M. and Schoepfle, C S Triphenylmethyl (XXIX) properties of diphenyl-α-naphthylmethyl 1655
Gray, H. See Wildman, E. A.
Greenwald, I. Supposed occurrence of methylguanidine in meat, with observations on the oxidation of creatine by $Hg(OAc)_2$ 1109
Greider, H. W. See Dains, F. B.
Griffiths, E. H Methods of measuring temp. (book rev.) 850

Hageman, A. M Chemistry of Te sulfide, 329, prepn. of certain org salts of Te 342
Hale, W. J. Four-membered cyclic-ureas (I) history and nomenclature 370
Hale, W. J. and Britton, E. C Prepn. of β-amino-propiophenone, 841, condensation of β-amino-propiophenone with nitromalonic aldehyde 1020
Hale, W J. and Honan, E. M Condensation of amino compds with nitromalonic aldehyde. 770
Hale, W. J. and Lange, N A. Four-membered cyclic-ureas (II) condensation of isocyanic acid with a Schiff base 379
Hall, R. E. and Adams, L H. Application of the thermionic amplifier to cond. measurements 1515
Halverson, J O. Modified Benedict method for the estn of S in feeds, feces and foods 1494
Halverson, J. O. and Schulz, J. A. Action of 10% thymol-$CHCl_3$ preservative on the Cl content of urine 440
Hamilton, H. C Digitalis leaves—effect on activity of temp in drying 125
Harding, E A and Smith, D. P. Occlusion of H and O by metal electrodes 1892, 1897
Harger, R N. Prepn of metol 270
Harkins, W. D. and Brown, F E. Detn of surface tension (free surface energy), and the wt. of falling drops—surface tension of water and benzene by the capillary height method. 499
Harkins, W. D. and Ewing, D T. Effects of acids and bases on the surface-energy relations of β,β'-dichloroethyl sulfide 1977
Harkins, W. D. and King, H H Electromagnetic hypothesis of the kinetics of heterogeneous equil., the structure of liquids, and cohesion 970
Harkins, W. D. and Paine, H. M Intermediate and complex ions (V) soly product and activity of the ions in bi-bivalent salts 1155
Harned, H. S Neutral salt catalysis (correction) 1092
Harris, B. R. See Curtman, L. J
Harris, C. P. See Bogert, M. T.
Harvey, A. W. See Pratt, D. S.
Hawse, V. P. See Hoffman, E. J.
Heidelberger, M. See Jacobs, W. A.
Heidelberger, M. and Jacobs, W. A. Synthesis in the cinchona series (I) simpler cinchona alkaloids and their dihydro derivs., 817; (II) quaternary salts, 2090; (III) azo dyes derived from hydrocupreine and hydrocupreidine, 2131; certain amino and acylamino phenol ethers 1450
Hendrixson, W. S. Lab. Manual of General Chemistry (book rev.) 130
Herman, A. G. See Tolman, R. C.
Heyl, F. W. Protein ext. of ragweed pollen, 670; yellow coloring substances of ragweed pollen 1285
Hildebrand, J. H. Soly. (III) relative values of internal pressures and their practical application 1067
Hirst, C. T. See Porter, C. W.
Hoffman, E. J. and Dame, P. A. Prepn. of hexanitro-diphenylamine from chlorobenzene 1013
Hoffman, E. J. and Hawse, V. P. Nitration of sucrose—sucrose octanitrate 235
Holmes, H. N. and Fall, P. H. Influence of the age of ferric arsenate on its peptization, 713; jellies by slow neutralization 763
Holmes, H. N., Kaufmann, W. E. and Nicholas, H. O. Vibration and syneresis of silicic acid gels 1329
Holmes, M. E. See Browne, A. W.
Honan, E. M. See Hale, W. J.

Hopkins, B. S. See Kremers, H. C.
Horsch, W. G. Potentials of the Zn and Cd electrodes.......... 1787
Hostetter, J. C. HCl color method for detg. Fe.......... 1531
Hostetter, J. C. and Roberts, H. S. Electrometric titrations, with special reference to the detn. of ferrous and ferric Fe.......... 1337
Hudson, C. S. and Komatsu, S. Rotatory powers of the amides of several α-hydroxy acids of the sugar group.......... 1141
Hudson, C. S. and Monroe, K. P. Amide of α-*d*-mannoheptonic acid.......... 1140
Hull, A. W. New method of chem. analysis.......... 1168
Hutchinson, G. F. See Pratt, D. S.

Jacobs, W. A. See Heidelberger, M.
Jacobs, W. A. and Heidelberger, M. Isomeric hydroxyphenyl-arsonic acids and the direct arsenation of phenol, 1440; aromatic As compds. (I) plan of procedure for the synthesis of arsenicals for chemotherapeutic research, 1581; (II) amides and alkylamines of *N*-arylglycine-arsonic acids, 1587; (III) ureides and substituted ureides of *N*-arylglycine-arsonic acids, 1600; (IV) aromatic amides of *N*-arylglycine-arsonic acid, 1610, (V) *N*-substituted glycylarsanilic acids, 1809; (VI) *N*-(phenyl-4-arsonic acid)-α-phenylglycine and its amides, 1822; (VII) substituted benzyl, phenoxyethyl, and phenacyl-arsanilic acids, 1826; (VIII) amides of (4-arsonic acid)-phenoxyacetic acid and the isomeric phenoxyacetyl-arsanilic acids.......... 1834
Jacobs, W A., Heidelberger, M. and Rolf, I. P. Certain aromatic amines and chloroacetyl derivs.......... 458
Jacobson, C. A. Alfalfa investigation (VII) alfalfa saponin.......... 640
James, C. See Brinton, P. H M.-P.; Fogg, H. C.
Jennings, W. L. and Scott, W. B. Prepn. of cyanogen chloride.......... 1241
Jodidi, S. L. and Moulton, S C. Cause of and remedy for certain inaccuracies in Hausmann's N distribution method.......... 1526
Johnson, T. B. and Daschavsky, P. G. Proteins (VI) destructive distn. of fibroin.......... 1147
Johnson, T. B and Matsuo, I. Pyrimidines (LXXXVII) alkylation of 5-amino-uracil.......... 78
Johnson, T. B. and Mikeska, L. A. Pyrimidines (LXXXVIII) Synthesis of cytosine aldehyde.......... 810
Johnston, J. See Adams, L. H.
Jones, W. N. See *Kohler*, E. P

Kamm, O. See Marvel, C. S
Kasiwagi, I. See Shibata, K.
Kaufmann, W. E See Holmes, H. N.
Kelley, G. L. and Bohn, R. T. Electrometric method for the detn. of ferrocyanides depending on a change in oxidation potential.......... 177
Kendall, E. C. Use of coal as a substitute for talcum to induce rapid boiling.......... 118
Kennedy, C. Forms of N in protein-free milk.......... 38
Keyes, F. G. and Felsing, W. A Equation of state for liquids and vapors (I) vapor phase of ethyl ether.......... 58
Kidwell, C. H. See Dains, F. B.
King, H. H. See Harkins, W D.
King, J. S. See Browne, A. W.
Kirschman, H D. See Bates, S. J.
Knowles, H. B. See Lundell, G. E. F
Kober, P. A. Prepn. of arsphenamine.......... 44
Kober, P A. and Davis, W. S. Prepn. of primary and secondary arsanilic acids.......... 4
Kohler, E. P. and Davis, T. L. Studies in the cyclopropane series (IV).......... 9
Kohler, E. P. and Engelbrecht, H. Addition of nitromethane to unsatd. esters, 764; studies in the cyclopropane series (VII) nitrocyclopropanes.......... 13
Kohler, E. P. and Gilman, H. Bromination and Br derivs. of certain ketonic esters.......... 6
Kohler, E. P. and Jones, W. N. Studies in the cyclopropane series (VI).......... 12
Kohler, E. P. and Rao, M. S. Studies in the cyclopropane series (IX) nitrocyclopropane derivs.......... 16
Kohler, E. P. and Steele, L. L. Studies in the cyclopropane series (V), 1093; colored condensation products from ketonic pyrazoline derivs.......... 11
Kohler, E. P. and Williams, H. R. Studies in the cyclopropane series (VIII) nitrocyclopropane derivs.......... 16
Kokatnur, V. R. Influence of catalysts on the chlorination of hydrocarbons.......... 1
Koller, J. P. See Dennis, L. M.
Komatsu, S. See Hudson, C. S.
Kremers, H. C. and Hopkins, B. S. Rare earths (IX) at. wt. of Yt..........

Krieble, V. K and Mangum, A W Estn of sulfates in a concd electrolyte and the detn of S in foods . . 1317

LAIRD, J S. and Simpson, T C Detn of HNO_3 and nitrites 524
Lamb, A B. and Larson, A. T Rapid detn of CO in air 1908
Lange, N A See Hale, W J
Langmuir, I Chem. reactions at low pressures (IV) cleanup of N by a heated Mo filament, 167, arrangement of electrons in atoms and mols 868 isomorphism isosterism and covalence 1543
Larson, A T See Lamb, A B
Leavell, G See Cadwell, S M
Lewis, G. N and Linhart, G A Degree of ionization of very dil electrolytes 1951
Lewis, W C McC System of Physical Chemistry (III) Quantum Theory (book rev) 1474
Liang, C L See Walton, J H
Lincoln, A. T. Textbook of Physical Chemistry (book rev) 1475
Lind, S C Chem action produced by Ra emanation (I) combination of H and O 531 (II) chem effect of recoil atoms 551
Linhart, G A. Applicability of the pptd Ag AgCl electrode to the measurement of the activity of HCl in extremely dil solns , 1175, see Lewis G N
Lipka, J Graphical and Mechanical Computation (book rev) 711
Lovelace, B F and Thomas C C Annual Chem Directory of the U S (book rev) 296
Lowy, A Modified graphic formulas for org cyclic compds 1029
Lundell, G E F and Knowles H B Detn of Zr by the phosphate method 1801
Lunn, A C Some formulas concerning surface tension 620
Lynn, E V Optically active pinene nitrosochloride and synthetical active pinene 361, new reaction of paraffin hydrocarbons 368

MAAS, O Automatic variations of gas pressure and its application to a vacuum pump, circulation of gases magnetic stirrer 53
Mabery, C F Genesis of petroleum as revealed by its N constituents 1690
MacArthur, C. G Method of tissue analysis—applied to the posterior and anterior lobes of cattle pituitaries 1225
McCoy, H N and Cartledge G H Gamma ray activity of Th D 50
MacDougall, F H Calcn of the temp coeff of the distribution ratio 1718
MacInnes, D A Activities of the ions of strong electrolytes, 1086 (correction) 1378
MacInnes, D A. and Adler, L H overvoltage 194
MacInnes, D A and Contieri, A W H overvoltage (II) applications of its variation with pressure to reduction, metal soln and deposition 2013
MacKenzie, A A. See Bray, W C
Maclean, H Lecithin and Allied Substances, the Lipines (book rev) 853
Mangum, A. W See Krieble, V K
Marcus, J K. See Bogert, M T
Marvel, C. S. and Kamm, O Org chem reagents (III) β-phenylhydroxylamine and cupferron . . . 276
Matsuo, I See Johnson, T B
Menzies, A W C. Vapor pressure of tetranitromethane, 1336, vapor pressures of Hg in the range 120° to 250° 1783
Merker, H M See Davis, L.
Michael, A. Relations between the chem structures of carbonyl derivs and their reactivities toward salts of semicarbazide 393
Mikeska, L A See Johnson, T B
Mitchell, C. A. Edible Oils and Fats (book rev) 476
Mitter, H. K. See Datta, R L.
Monroe, K. P. Prepn. of xylose from corn cobs, 1002, see Hudson, C S.
Moore, F. J. History of Chemistry (book rev) 853
Moore, R. W. Growing large perfect crystals from soln 1060
Moore, W. C. Emulsification of water and of NH_4Cl solns. by means of lamp black . 940
Moulton, S. C. See Jodidi, S. L.
Mueller, E. F. and Burgess, H. A. Standardization of the S b p 745
Mulliken, R. S. See Tolman, R C
Mullanix, R. D. See Schlesinger, H I
Myers, R G. See Oertly, E.

NELSON, E. K. Constitution of capsaicin, the pungent principle of *Capsicum*, 1113, (correction), 1472, vanillyl acylamides . .

Nelson J M and Beegle F M Mutarotation of glucose and fructose 559
Neogi, P Space representation of org N compds 622
Neun D E See Sherman H C
Newbery E Occlusion of H and O by metal electrodes 1887, 1895
Nicholas, H O See Holmes H N

Oertly E and Myers, R G New theory relating constitution to taste, 855, (correction) 1378
Okey R E See Beal, G D

Paine, H M See Harkins W D
Palitzsch, S Compressibility of aq solns of casein and peptone 346 see Richards T W
Peirce W McG See Tolman R C
Peters C A Prepn of Substances Important in Agriculture—Lab Manual of Synthetic Agricultural Chemistry (book rev) 1876
Pettijohn E Measurement of the thickness of film formed on glass and sand 477
Porter, C W and Borgstrom P Tetraphenyldiarsine 2048
Porter C W and Hirst C T Asymmetric dyes 1264
Porter L E and Browning P E Sulfite method for the sepn and detn of Ga when associated with Zn 1491
Power F B and Chesnut, V K Detn of caffeine in vegetable material 1298 *Ilex vomitoria* as a native source of caffeine 1307
Pratt D S Doane F B and Harvey A W Phthalic acid derivs —constitution and color (XVI) phenoltetrabromo-phthalein and some of its derivs 1289
Pratt D S Hutchinson G F and Harvey A W Phthalic acid derivs —constitution and color (XVII) tetrabromo-fluorescein tetrabromo-eosin and some of their derivs 1293

Raiford L C Mol rearrangement in the acylation of certain aminophenols 2068
Rao M S See Kohler E P
Rather J B and Reid E E Identification of acids (IV) phenacyl esters 75
Read J W See Washburn E W
Reed, F H See Schlesinger, H I
Reedy J H Electrolytic detn of the halogens 1898
Reid E E See Rather J B
Reyerson L H See Tolman R C
Richards T W and Boyer S Purification of Ga by electrolysis and the compressibility and d of Ga 133
Richards T W Carver E K and Schumb, W C Effect of pressure and of dissolved air and water on the m p of benzene 2019
Richards T W Craig W M and Sameshima J Purification by sublimation and the analysis of gallium chloride 131
Richards T W and Daniels F Concd Th amalgams—their electrochem and thermochem behavior densities and f ps 1732
Richards T W and Palitzsch S Compressibility of aq solns especially of urethan and the polymerization of water 59
Richards, T W and Shipley, J W Dielec consts of typical aliphatic and aromatic hydrocarbons cyclohexane cyclohexanone and cyclohexanol 2002
Richter, V von Org Chemistry (book rev) 2148
Rindfusz R E Syntheses of chromanes and coumaranes 665, see Adams, R
Roberts, H S Elec app for use in electrometric titration 1358, see Hostetter, J C
Rockwood, E W Effect of neutral salts on the activity of ptyalin 228
Rolf, I P See Jacobs W A
Ross, W H and Trumbull, H L Analysis of mixts of ethylene and acetylene 1180
Rouiller, C A Some metallic derivs of ethyl thioglycollate 777

Sameshima, J See Richards T W
Sarkar, B K Hindu Achievements in Exact Science (book rev) . 475
Scatchard, G See Bogert, M T , Smith, A
Schlesinger, H I and Bunting, E N Cond (VII) transference numbers of the formates of Na, K and Ca in anhydrous formic acid . 1934
Schlesinger, H I and Mullinix, R D Cond (IV) cond of alk earth formates in anhydrous formic acid . 72
Schlesinger, H I and Reed, F H Cond [illegible]) measurement of the cond. of solns , 1727, cond. (VI) behavior of mixts of 2 salts contg. a common ion in anhydrous formic acid soln 1921
Schoepfle, C S See Gomberg, M.
Schulz, J A. See Halverson, J O

Schumb, W C. See Richards, T W

Scott, J W See Wheeler, A S

Scott, W B See Jennings, W L

Sherman, H C Chemistry of Food and Nutrition (book rev) 847

Sherman, H C and Neun, D E Proteolytic activity of pancreatic amylase prepns 1855

Sherman, H C Thomas, A W and Baldwin M E Influence of H ion concn on enzymic activity of 3 typical amylases 231

Sherman, H C and Walker, F Influence of aspartic acid and asparagin on the enzymic hydrolysis of starch 1866

Sherman, H C, Walker, F and Caldwell M L Action of enzymes on starches of different origin 1123

Shibata, K, Shibata, Y and Kasiwagi I Studies on anthocyanins—color variation in anthocyanins 208

Shibata, Y See Shibata K.

Shipley, J W See Richards T W

Simpson, M E See Bray, W C

Simpson, T C See Laird J S

Small, J C Detn of sol starch in the presence of starch and its hydrolytic cleavage products, 107, prepn of sol starch 113

Smith, A Intermediate Text-Book of Chemistry (book rev) 1704

Smith, A, Eastlack, H and Scatchard, G Transition of dry NH_4Cl 1961

Smith C R Mutarotation of gelatin and its significance in gelation 135

Smith, D P See Harding, E A

Smith, E F James Woodhouse a Pioneer in Chemistry (book rev) 710 Chemistry in Old Philadelphia (book rev) 1313 (correction) 1704

Smith, S C See Wheeler A S

Smithey, I W See Venable F P

Smyth H DeW See Tolman R C

Spitzer G Carr R H and Epple W F Soft corn—its chem compn and N distribution 1212

Steele, L L See Kohler, E P

Stoddard, J T Introduction to Org Chemistry (book rev 1705

Strong W W New Science of the Fundamental Physics (book rev) 851

THING, C W See Byers H G

Thomas, A. W See Sherman H C

Thomas, A W and Baldwin M E Contrasting effects of chlorides and sulfates on the H ion concn of acid solns 1981

Thomas, C C See Lovelace, B F

Thorpe, T E See Clarke F W

Tolman, R C and Bracewell R S Mol mechanism of colloidal behavior (II) swelling of fibrin in alkalies 1503

Tolman, R C, Gerke, R H, Brooks A P Herman A G Mulliken R S and Smyth, H DeW Relation between intensity of Tyndall beam and size of particles 575

Tolman, R C Reyerson L H, Brooks A P and Smyth H D Elec precipitator for analyzing smokes 587

Tolman, R C Reyerson L H, Vliet, E B, Gerke R H and Brooks A P Relation between the intensity of Tyndall bean and concn. of suspensions and smokes 300

Tolman, R C and Vliet E B Tyndallmeter for the examn of disperse systems 297

Tolman, R C, Vliet, E B Peirce W McG and Dougherty R H Disappearance of smoke in a confined space 304

Trumbull, H L See Ross, W H

URBAIN, G See Clarke, F W

VARMA, P S See Datta, R L

Venable, F P and Smithey, I W Zirconyl compds with the oxy halogen acids 1722

Vliet, E B See Tolman, R C

Voorhees, V See Adams R

WAKEMAN, N A Reduction of dihydroxy-thymoquinone by means of Pd-H 1873

Walker, F See Sherman, H C

Walton, J H and Liang, C L New addition compds of quinoline with certain inorg salts 1027

Ware, G M See Fales, H A

Washburn, E W and Read, J W Laws of "concd" solns (VI) general b p law 729

Watson, E R Color in Relation to Chem Constitution (book rev) 710

Wells, P. V. and Gerke, R. H. Oscillation method for measuring the size of ultramicroscopic particles........ 312
Wheeler, A. S. and Scott, J. W. Halogenation of juglone—new type of naphthalene dyes... 833
Wheeler, A. S. and Smith, S. C. Action of basic reagents on Schiff's bases (I) chloralnitraniline group........ 1862
White, E. C. and Acree, S. F. Quinone-phenolate theory of indicators—reactions of phenolsulfonephthalein, and its bromo and nitro derivs., and their monobasic and dibasic salts.... 1190
Whitmore, F. C. Org. Hg compds. derived from *p*-bromodimethylaniline........ 1841
Wildman, E. A. and Gray, H. Prepn. of 1,2-dichloroether........ 1122
Williams, H. E. See Kohler, E P.
Williamson, E. D. See *Adams*, L. H.
Wilson, J. A. Retardation by sugars of diffusion of acids in gels........ 358
Witzemann, E. Volatility with steam of lower fatty acids in dil. aq. solns........ 1946

Subject Index to Volume XLI, 1919.

ACETALDEHYDE, oxidation of ... 1385
4-Acetamino-5-ethoxyphenol ... 1468
4-Acetamino-6-ethoxyphenol ... 1459
4-Acetaminoguaiacol ... 1460
3-Acetamino-6-methoxy-benzenesulfonamide ... 1456
3-Acetamino-6-methoxy-benzenesulfonic acid ... 1456
4-Acetamino-5-methoxyphenol ... 1466
m-Acetamino-phenoxyacetic acid ... 465
Acetamino-resacetophenone ... 265
Acetic acid, detn. *of*, 1269; volatility with steam of dil aq soln ... 1946
Acetophenetide, new, derived from the ethyl ether of syringic acid ... 798
2′-Acetoxyflavone ... 96
3′-Acetoxyflavone ... 96
4′-Acetoxyflavone ... 97
Acetyl-*o*-allyl-*o*-cresol, and dibromide ... 662
Acetyl-*o*-allyl-*p*-cresol, and dibromide ... 661
Acetyl-*α*-allyl-*β*-naphthol, and dibromide ... 663
Acetyl-*o*-allylphenol, and dibromide ... 654
2-Acetylamino-4,6-dibromophenol ... 2076
2-Acetylamino-4,6-dibromophenyl acetate ... 2075
2-Acetylamino-4-methyl-6-bromophenol ... 2073
2-Acetylamino-4-methyl-6-bromophenyl acetate ... 2072
Acetyl-2-bromojuglone ... 838
Acetyl-2-chlorojuglone ... 836
Acetyl-dichlorojuglone ... 837
3-Acetyl-1,4-diphenyluretidone ... 385
Acetylene, analysis of mixts of ethylene and ... 1180
Acetyl-resacetophenone, nitration of ... 264
Acetyltribromojuglone ... 839
Acids, identification of, 75; retardation by sugars of diffusion of, in gels, 358; chem. nature of the adsorption of, by the protein mol., 1511; effects on the surface energy relations of *β*,*β*′-dichloroethyl sulfide, 1977, contrasting effects of chlorides and sulfates on the H-ion concn. *of* ... 1981
Acylation, mol. rearrangement in the, of certain aminophenols ... 2068
Addition, some factors bearing on 1,6- ... 1132
Adsorption, at interfaces, 981; chem. nature of the, of acids and alkalies by the protein mol. ... 1511
Affinity, spectrophotometric method for measuring the equil. and, consts. of the phenolphthaleins and phenolsulfonephthaleins ... 1031
Agricultural chemistry, Lab. Manual of Synthetic (Peters, book review) ... 1876
Agriculture, Prepn. of Substances Important in (Peters, book review) ... 1876
Air, detn. of CO in ... 1908
β-Alanine, ethyl ester hydrochloride, 774; methyl ester hydrochloride ... 775
Alcohols, prepn. and hydrolysis of esters derived from the substituted aliphatic ... 424
Aldehydes ... 421
Alfalfa, saponin ... 640
Alizarin, metallic derivs. of ... 2082
Alkalies, swelling of fibrin in, 1503; chem. nature of the adsorption of, by the protein mol ... 1511
Alkaline earth formates, cond. of, in anhydrous formic acid ... 72
Alkylamides, of *N*-arylglycine-arsonic acids ... 1587
Alkylation, of 5-amino-uracil ... 782
Alkyl iodides, prepn. of ... 789
Allophanic acid, di-silver salt of ethyl ester of ... 1005
o-Allylanisole ... 659
o-Allyl-*o*-cresol ... 662
o-Allyl-*p*-cresol ... 661
Allyl-*β*-naphthol ... 663
o-Allylphenols, cyclic ethers from ... 648
Aloes ... 704
Amalgams, concd. thallium ... 1732
Amides, rotatory powers of the, of several *α*-hydroxy acids of the sugar group, 1141; of *N*-aryl-

glycine-arsonic acids, 1587; aromatic, of *N*-arylglycine-arsonic acids, 1610; of (4-arsonic *acid)-phenoxyacetic acid and the isomeric phenoxyacetyl-arsanilic acids* *1834*
Amine oxides 633
Amines, certain aromatic, and chloroacetyl derivs, 458; action on the substituted ureas and urethanes 1004
Aminobenzoylene-ureas, synthesis of certain 2052
Amino compounds, condensation, with nitromalonic aldehyde 770
p-Aminodiphenyl-methylcarbinol 1265
4-Amino-5-ethoxyphenol 1467
4-Amino-6-ethoxyphenol 1459
Aminoflavones, synthesis of 83
4-Aminoguaiacol 467
3-Amino-6-methoxy-benzenesulfonamide 1457
4-Amino-5-methoxyphenol 1466
2-Amino-4.-methyl-6-bromophenol *2072*
Aminophenol 264
Aminophenols, prepn of, 436; mol. rearrangement in the acylation of certain 2068
m-Aminophenyl-arsonic acid, derivs o 1598
o-Aminophenyl-arsonic acid, derivs of 1598
p-Aminophenyl-arsonic acid, 452, derivs of 1589
β-Amino-propiophenone, prepn of, 841, hydrochloride, 846; condensation with nitromalonic aldehyde 1020
4-Aminopyrocatechol, hydrobromide, 467, 468, derivs of the ethers of *1457*
Aminotolyl-arsonic acids, derivs. of 1599
5-Amino-uracil, alkylation of, 782, prepn and alkylation of 784, 785
4-Aminoveratrol 1460
Ammonates, of copper selenate 965
Ammonia, detn in ammonates of Cu selenate, 967, action on the substituted ureas and urethanes, 1004; behavior of the hydronitrogens and their derivs. in liquid 1769
Ammonium chloride, emulsification of water and of, solns by means of lamp black, 940, transition *of dry* 1961
Ammonium compounds, number of isomers of org, 627; cyclic 638
Ammonium trinitride, electrolytic nitridation of various anodes in a soln. of 1769
Amplifier, application of the thermionic, to cond. measurements 1515
Amylases, influence of H-ion concn on enzymic activity of 3 typical, 231; proteolytic activity of pancreatic, prepns 1855
Analysis, identification of acids, 75; arsenious oxide as a standard substance in iodimetry, 351; new method of chem, 1168, electrometric titrations, 1337, elec app. for use in electrometric *titration, 1358, Advanced Course in Quant. (Fay, book review), 1472;* electrometric *1776*
Anhydrides, condensation of 1-phenyl-3-methyl-5-pyrazolone with 707
Anhydrophthalyl-*bis*-1,3-diketohydrindene 1224
Anisole, nitro deriv. of 2043
Anisole-sulfonic acid, action of Cl on 2030
Anodes, electrolytic nitridation of various, in a soln. of NH_4N_3 1769
Anthocyanins, color variation in 208
Anthraquinone, nitro deriv. of 2048
Arsanilic acids, prepn. of primary and secondary, 451; derivs. of, 1601, 1608, 1609, 1613, 1638, 1640, 1642, 1809, 1826 1834
Arsenation, direct, of phenol 1440
Arsenic acid, interaction of phenol and 432
Arsenic compounds, aromatic, 1581, 1587, 1600, 1610, 1809, 1822, 1826 1834
Arsenious oxide, as a standard substance in iodimetry 351
(4-Arsonic acid)-phenoxyacetic acid, amides of 1834
Arsphenamine, prepn. of 442
N-Arylglycine-arsonic acids, amides and alkylamides of, 1587; ureides and β-substituted ureides of, 1600; aromatic amides of 1610
Asparagine, influence on the enzymic hydrolysis of starch 1866
Aspartic acid, influence of, on the anzymic hydrolysis of starch 1866
Asymmetric atoms, combination of asymmetric N, with asymmetric C and N atoms 634
Atomic weights, rept. of the intern. comm. on, for 1919–20 1881
Atoms, arrangement of electrons in, 868; chem. effect of recoil 551
Auxogluc 859

BACTERIA, gentian violet and 2083
Bases, effect on the surface energy *relations of β,β′*-dichloroethyl sulfide 1977

Benzaldehyde, condensation with phenylurea 385, 386
β-Benzal-β-nitro-ethyl tertiarybutyl ketone 1703
Benzene, surface tension, 499; adsorption of the interface water-, as compared with that on the surface of the water, 990; effect of pressure, and of dissolved air and water on the m. p. of. 2019
Benzoic acid, iodinization of 294
Benzoylacrylic acid, methyl ester of, addition of Na nitromethane to, 767; ester, prepn. of, 768
2-Benzoylamino-4, 6-dibromophenyl acetate 2077
2-Benzoylamino-4-methyl-6-bromophenyl acetate 2071, 2074
2-Benzoylamino-phenyl acetate 2078
Benzoyl-*p*-bromo-*o*-allylphenol, and derivs. 660
2-Benzoyl-4-bromo-3,5-diphenylfurane 1262
2-Benzoyl-1,3-diketohydrindene 1223
2-Benzoyl-3,5-diphenylfurane 1262
Benzoylene-urea, and Na salt 2056, 2058
2-Benzoyl-α ethylamino-2-benzoyl-γ-ethylimino-β-nitropropylene 1024
2-Benzoyl-β-ethylamino-α-nitro-acrolein 1024
Benzoylphenyl-dimethyl butyrate, prepn of 686
1-Benzoyl-2-phenyl-3-nitrocylcopropane 1381
γ-Benzoyl-β-phenylpropyl-malonic acid, and dimethyl ester 995, 996
γ-Benzoyl-β-phenylvaleric acid, and Me ester 996
Benzoylpropionic acid, prepn of 768
Benzylarsanilic acid, substituted 1826
2-Benzyl-3,5-dipheny furane 1262
Benzyliden-aniline, condensation with isocyanic acid 384
Benzylidenebisphenylureide 385
Benzylidene-ethylamine, condensation of isocyanic acid and 387
3-Benzyl-5-tertiarybutyl-isoxazole 1703
5-Benzyl-3-tertiarybutyl-isoxazole 1703
Biography, James Woodhouse (Smith, book review) 710
Biuret 1006
Boiling, use of coal as a substitute for talcum to induce rapid 1189
Boiling points, detn. of solns., 721; laws of "concd" solns.—general b. p. law 729
Books, New: Reviews—Chemistry—First Stage (Armitage), 130, Lab. Manual of General Chemistry (Hendrixson), 130; Annual Chem. Directory of the U. S (Lovelace and Thomas), 296, Chem. French (Dolt), 474, Hindu Achievements in Exact Science (Sarkar), 475; Edible Oils and Fats (Mitchell), 476, Color in Relation to Chem Constitution (Watson), 710; James Woodhouse, a Pioneer in Chemistry (Smith), 710, Graphical and Mechanical Computation (Lipka), 711; Chemistry of Food and Nutrition (Sherman), 847; Methods of Measuring Temp (Griffiths), 850; New Science of the Fundamental Physics (Strong), 851; History of Chemistry (Moore), 853; Lecithin and Allied Substances, the Lipines (MacLean), 853; Helvetica Chimica Acta, 1150; Chemistry in Old Philadelphia (Smith), 1313; Essentials of Modern Chemistry (Dull), 1314, Chem. Analysis of Fe (Blair), 1315; Advanced Course in Quant. Analysis (Fay), 1472, System of Phys. Chemistry (Lewis), 1474; Textbook of Physical Chemistry (Lincoln), 1475; Chemistry in Old Philadelphia (Smith), 1704; Intermediate Text-book of Chemistry (Smith), 1704; Introduction to Org. Chemistry (Stoddard), 1705; Prepn. of Substances Important in Agriculture (Peters), 1876; Introduction à la Chimie Générale (Copaux), 1877, Chimica delle sostanze esplosive (Giua), 1878; Org. Chemistry for Advanced Students (Cohen), 2148, Org Chemistry, or Chemistry of the C Compds. (Richter), 2148
Bromination, of certain ketonic esters 683
2-Bromo-5-aminophenol 464
γ,γ-Bromobenzoyl-β-phenylpropyl-malonic acid, dimethyl ester 997
γ,γ-Bromobenzoyl-β-phenylvaleric acid 996
5-Bromobenzyl-3-tertiarybutyl-isoxazole 1704
***p*-Bromo-α-bromomethyl-coumarane** 658
2-Bromo-5-chloroacetyl-aminophenol 464
β-Bromocinnamic acid, Me ester 99
2-Bromo-3,5-dimethoxy-4-ethoxyacetanilide 806
***p*-Bromodimethylaniline, org. Hg compds. derived from-** 1841
β-Bromo-ethylphenyl ether, coumarane from 670
***p*-Bromo-iodobenzene** 294
2-Bromojuglone 838
***p*-Bromo-α-methylcoumarane** 657, 661
α-Bromomethyl-coumarane 655

p-Bromo-α-methylene-coumarane 661
α-Bromomethylene-coumarane 656
Bromopaeonol, and derivs. 261, 262
p-Bromophenol, derivs. of 660
Bromophenylnitro-ethylmalonic acid, methyl ester of 767
γ-Bromopropylphenyl ether, chromane from 669
Bromo-resodiacetophenone 267
Bumping, use of coal as a substitute for talcum to induce rapid boiling 1189
N-Butyl iodide, prepn. of 798
Butyric acid, molar activity and the assocn. of, in the vol. phases, 988; volatility with steam in dil. aq. soln. 1946

CADMIUM, potential of the, electrode 1787
Cadmium acetate, addition compd. with quinoline 1028
Cadmium alizarate 2082
Caffeine, detn. in vegetable material, 1298, *Ilex vomitoria* as native source of 1307
Calcium formate, transference number in anhydrous formic acid 1934
Capillary height method, surface tension of water and benzene by 499
Capsaicin, constitution of 1115, 1472
Capsicum, pungent principle of 1115
Carbethoxybiuret 1005
2-Carbethoxy-β-ethylamino-α-nitroacrolein 775
2-Carbomethoxy-β-ethylamino-α-nitroacrolein 776
Carbon, combination of asymmetric N with asymmetric, and N atoms 634
Carbon monoxide, detn. in air 1908
Carbonyl derivatives, relations between the chem. structures of, and their reactivities towards salts of semicarbazide 393
Carbonyldi-β-naphthyldiurea 1011
Carbonyldiurethane 1004
o-Carboxy-α-bromomethylene-coumarane 664
o-Carboxy-α-methylene-coumarane 664
Carvacrol-5-sulfonic acid, action of Cl on 2034
Cascara 703
Casein, compressibility of aq. solns. of 346
Catalysis, neutral salt 1092
Catalysts, influence on the chlorination of hydrocarbons 120
Cerium, detn. of, in the presence of other rare earths 1080
Chemical compounds, mechanism of chem. action and the structure and properties of 887
Chemical constitution, relations between the, of carbonyl derivs. and their reactivities toward salts of semicarbazide, 393; Color in Relation to (Watson, book review), 710; new theory relating, to taste, 855, 1378; phthalic acid derivs — and color 1289, 1293
Chemistry, First Stage (Armitage, book review), 130; Lab. Manual of General (Hendrixson, book review), 130; History of (Moore, book review), 853; Helvetica Chimica Acta (book review), 1150; in Old Philadelphia (Smith, book review) 1313, 1704; Essentials of Modern (Dull, book review), 1314; Intermediate Text-book of (Smith, book review), 1704; Introduction à la Chimie Générale (Copaux, book review) 1877
Chloralnitraniline group 1862
Chlorides, contrasting effects of, and sulfates on the H-ion concn. of acid solns. 1981
Chlorination, influence of catalysts on the, of hydrocarbons 120
Chlorine, action on hydrazine, hydroxylamine and urea, 124; action of 10% thymol-$CHCl_3$ preservative on the, content of urine, 440; replacement of sulfonic groups by 2028
Chloro-acetmethylamide 472
Chloro-acetpiperidide 473
Chloro-acet-*n*-propylamide, and hexamethylenetetrammonium salt 472, 473
p-Chloro-acetylaminoacetophenone 469
4-Chloro-acetylamino-5-ethoxyphenol 1468
4-Chloro-acetylamino-6-ethoxyphenol 1460
4-Chloro-acetylaminoguaiacol 1457
5-Chloro-acetylaminoguaiacol 1458
4-Chloro-acetylamino-6-hydroxy-benzenesulfonic acid 471
4-Chloro-acetylamino-5-methoxyphenol 1467
1-Chloro-acetylamino-2-naphthol 460
1-Chloro-acetylamino-4-naphthol 460
o-Chloro-acetylaminophenol 458
p-Chloro-acetylamino-phenolacetic acid 469

m-Chloro-acetylaminophenoxyacetic acid 466
o-Chloro-acetylaminophenyl acetate 458
4-Chloro-acetylamino-pyrocatechol 468
Chloro-acetyl-*m*-anisidine 1452
Chloro-acetyl-*o*-anisidine 1451
Chloro-acetylanthranilic acid, ethyl ester of 469
Chloro-acetyl derivatives, certain aromatic amines and 458
Chloro-acetyl-ethylurea 473
Chloro-acetyl-*N*-methylanthranilic acid, and Et ester 470
Chloro-acetyl-*m*-phenetidine 1452
Chloro-acetyl-*o*-phenetidine 1452
Chloro-acetyl-*p*-phenetidine 1453
Chloro-acetylsulfanilic acid, and sodium salt 470
Chloro-benzene, prepn. of hexanitro-diphenylamine from 1013
Chloro-derivatives, prepn. of org 2028
8-Chloro-2,3-dibromojuglone 840
Chloroform, action of 10% thymol-, preservative on the Cl content of urine 440
p-Chloroiodobenzene 293
2-Chlorojuglone 836
Chloromethylanthranilic acid, Na salt of 470
β-Chloropropionic acid, isoamyl ester 844
β-Chloropropiophenone 845
Chromanes, synthesis of 665
Chrysophanic acid 698
Cinchona alkaloids, simpler, and their dihydro derivs., 817; syntheses in the cinchona series, 817, 2090 2131
Cinchonidine, hydrochloride, 819; quaternary salts of 2094
Cinchonine, hydrochloride, 819; quaternary salts of 2092
Cinnamic acid, iodinization of 295
Cinnamylidene-malonic acid, dimethyl ester 767
Citric acid, Te acid salt 343
Coal, use as a substitute for talcum to induce rapid boiling 1189
Cobalt, passivity of 1902
Cohesion, 970, relation of the intensity of the intermol. electromagnetic field to, and valence ... 974
Colloids, mutarotation of gelatin and its significance in gelation, 135; tyndalimeter for the examn. of, 297; retardation by sugars of diffusion of acids in gels, 358; influence of the age of ferric arsenate on its peptization, 713; jellies by slow neutralization, 763; mol. mechanism of colloidal behavior—swelling of fibrin in alkalies, 1503; vibration and syneresis of silicic acid gels, 1329; mol. mechanism of colloidal behavior— chem. nature of the adsorption of acids and alkalies by the protein mol 1511
Color, variation in anthocyanins, 208; in Relation to Chem. Constitution (Watson, book review), 710; phthalic acid derivs —constitution and 1289, 1293
Coloring substances, yellow, of ragweed pollen 1285
Compressibility, detn. of, of solids at high pressures, 12, of aq. solns., especially of urethane, 59; of aq. solns. of casein and peptone 346
Computation, Graphical and Mechanical (Lipka, book review) 711
Condition equation, for liquids and vapors 689
Conductivity, electric, of alk. earth formates in anhydrous formic acid, 72, application of thermionic amplifier to, measurements, 1515; measurement of the, of solns., 1727, studies in, 1921 1934
Containers, permanent marking of glass vessels 359
Coördination number, valence, and covalence 926
Copper alizarate 2082
Copper chloride, action of CuCl with compds contg. the trichloromethyl group 1129
Copper selenate 949
Copper selenite, oxidation by Cl 956
Copper thiocyanate, addition compd. with quinoline 1028
Corn, soft, its chem compn. and N distribution 1212
Corn cobs, prepn. of xylose from 1002
Coumaranes, synthesis of 665
Covalence 1543
Crab grass, compn. of the ash of, as affected by the soil in which it is grown 1384
Creatine, oxidation by mercuric acetate 1109
m-Cresol, derivs of ethers of, 1451; nitro deriv. of 2041

o-Cresol derivs of, 662, derivs of ethers of, 1451, nitro derivs of 2040
p-Cresol derivs of 661, nitro deriv of 2041
o-Cresol-5-sulfonic acid action of Cl on 2032
m-Cresolsulfonic acids, action of Cl on 2033
p-Cresolsulfonic acids action of Cl on 2034
Crystals method of growing large perfect, from soln, 1060, new method of chem analysis 1168
Cupferron 276
Cuprous chloride etc See *Copper chlorides*, etc
Cyanide, liquid NH_3-Na method for halogens in org compds the formation of, and method of removing from the soln 1051
Cyanogen chloride prepn of 1241
Cyanuric acid 1006
Cyclic compounds modified graphic formulas for org 1029
Cyclohexane, dielec const of 2002
Cyclohenanol dielec const of 2002
Cyclohexanone dielec const of 2002
Cyclopropane series 992, 1093 1249 1379, 1644 1697
Cytosine aldehyde, synthesis of 810

2′-DIACETYL AMINOFLAVONE 94
3′-Diacetyl-aminoflavone 95
4′-Diacetyl-aminoflavone 95
Diacetyl 4 aminopyrocatechol 1463
6,8-Diamino-benzoyleneurea 2060
Di *p*-aminophenyl arsinic acid 454
1,2-Dibenzoyl 2 acetoxy 3 phenylcyclopropane 1261
1,2-Dibenzoyl-2 bromo-3-phenylcyclopropane 1261
1,2 Dibenzoyl 3 phenylcyclopropane and derivs 1253 1254
γ,γ Dibromo-γ nitro-β phenyl propyl (4-bromophenyl) ketone 1648
3,5-Dibromo-4-phenyl 6-(4-bromophenyl) dehydropyrone 1 2 1097
α-γ Dibromo-β phenylpropyl (4-bromophenyl) ketone 1653
2,4 Dichloro-5 acetaminophenol 460
2,4-Dichloro-5 acetanisidide 462
2,4-Dichloro-5-aminophenol 461
2,4-Dichloro-5-anisidine 462
2,4-Dichloro-5-chloroacetylamino-phenol 461
1,2-Dichloroether prepn of 1122
N,*N*′-β,β β-Dichloro-ethoxy-ethylidenebis-*o*-nitraniline 1864
N,*N*′-β β β-Dichloro-ethoxy-ethylidenebis-*p* nitraniline 1865
β β′ Dichloroethyl sulfide 1414 effects of acids and bases on the surface energy relations of 1977
N *N*′-β,β β-Dichloro-hydroxy-ethylidenebis-*o*-nitranilin 1863
2,3-Dichlorojuglone 837
N,*N*′-β,β,β-Dichloro-methoxy-ethylidenebis-*o*-nitraniline 1864
2,4-Dichloroquinazoline 2061
Dielectric constants, of typical aliphatic and aromatic hydrocarbons cyclohexane cyclohexanone and cyclohexanol 2002
2 4-Diethoxyacetanilide 1471
3,4-Diethoxyacetanilide 1464
γ-Diethoxy-acetoacetic acid ethyl ester of 812
2,4-Diethoxyaniline 1471
3,4-Diethoxyaniline 1465
2,4-Diethoxychloro-acetanilide 1472
3,4-Diethoxychloro-acetanilide 1465
Diffusion retardation by sugars of of acids in gels 358
Digitalis, leaves—effect on activity of temp in drying 125
Digitaria sanguinalis 1384
o,*p*′(?)-Dihydroxy-diphenylarsonic acid 1449
p,*p*′-Dihydroxy-diphenylarsonic acid 1448
p-Di(hydroxy-isopropyl)benzene 1680
Dihydroxythymoquinone, reduction by means of Pd-H 1873
p-Diiodobenzene 293
1,4-Diisopropenylbenzene 1682
1,4-Diisopropenyl-$\Delta^{1,4}$-dihydrobenzene 1683
1,4-Diisopropylcyclohexane, derivs of 1676

Diketohydrindene 1221
3,5-Dimethoxy-*p*-acetophenetide 805
2,4-Dimethoxyaniline 1468
2,4-Dimethoxychloro-acetanilide 1469
3,4-Dimethoxychloro-acetanilide 1461
3,5-Dimethoxy-4-ethoxybenzene-azo-β-naphthol 809
3,5-Dimethoxy-4-ethoxy *s*-diphenylurea 808
3,5-Dimethoxy-4-ethoxy-iodobenzene 807
3,5-Dimethoxy-4-ethoxy phenylurea 808
3,5-Dimethoxy *p* phenetidine 803
2,4-Dimethoxy-quinazoline 2061
1,3-Dimethyl-5 aminouracil 785, 788
1,3-Dimethyl-benzoylene-urea 2062
α,α-Dimethyl-β-phenyl γ-benzoylbutyric acid and oxime 687, 690
α,α-Dimethyl-β-phenyl γ-benzoylcrotolactone 689
α,α-Dimethyl-β-phenyl γ-(phenylglyoxyl)propionic acid, ethyl ester of 691
Di-α-naphthylbiuret 1011
Dinitro-acetyl-resacetophenone 265
6,8-Dinitrobenzoyleneurea and salts 2059
Dinitrochlorobenzene 1015
3,5-Dinitro-*o*-cresol 2045
3,5-Dinitro-*p*-cresol 2046
Dinitro-diphenylamine 1016
Dinitro-resacetophenone and phenylhydrazone 265
2,5-Diphenyl 4-(α-acetoxybenzyl)furane 1255
1,4-Diphenyl 2-benzoyl-4-chlorobutadiene 1260
2,5-Diphenyl-4-benzoylfurane and oxime 1257, 1258
Diphenylbiuret 1007
2,5-Diphenyl-3-bromo-4-benzoylfurane *1257*
2,5-Diphenyl-4-(α-bromobenzyl)furane 1255
2,4-Diphenylbutene-3 acid 1 and Me ester 1137, 1138
1,2-Diphenylcarbinyl 3 phenylcyclopropane 1259
1,4-Diphenyl-1 4-dichloro-3-benzoyl butene 4 1259
2 5 Diphenylfurane carboxanilide 1258
3,5-Diphenylfurane-carboxanilide 2 1263
2,5-Diphenylfurane carboxylic acid 4 1258
3,5-Diphenylfurane-carboxylic acid 2 1263
2,5-Diphenyl-4-(α hydroxybenzyl)furane 1256
2,4-Diphenyl-4-hydroxy-1,1-butanedicarboxylic acid 1136
β,δ-Diphenyl-δ-hydroxybutyric acid, and lactone 1135 1136 1138
Diphenylmethyl-carbinol-*p*-azodimethylaniline 1265
Diphenylmethyl-carbinol *p*-azo-β-naphthol 1265
Diphenyl-α-naphthylmethyl, properties of 1655
4,6-Diphenylpyrone-1,2 1100
1,4-Diphenyluretidone 384
Directory, Annual Chem of the U S (Lovelace and Thomas book review) 296
Disperse systems, tyndallmeter for the examn of 297
Distribution ratio, calcn of the temp coeff of the, 1718, relations between, temp and concn in system water–ether–succinic acid 1721
Di-*o*-tolylbiuret . 1009
Drops, detn of surface tension and the wt of falling 499
Drop-weight apparatus . 507
Dyes, synthesis of flavone-azo-β-naphthol, 83, new type of naphthalene, 833, asymmetric, 1264, azo, derived from hydrocupreine and hydrocupreidine 2131

ENERGY, free, of the H halides in aq soln — free, of formation of HCl . 1991
Electrical apparatus, for use in electrometric titration . 1358
Electrical precipitator, for analysing smokes 587
Electrodeposition, H overvoltage—applications of its variation with pressure to, of metals . 2013
Electrodes, normal H *vs* the normal calomel, 1090, applicability of the pptd Ag AgCl, to the measurement of the activity of HCl in extremely dil solns , 1175, potentials of the Zn and Cd, 1787; occlusion of H and O by metal, 1887, 1892, 1895 . 1897
Electrolytes, activities of the ions of strong 1086, 1378, degree of ionization of very dil 1951
Electrons, arrangement in atoms and mols 868

Emodin methyl ether.......... 698
Emulsification, of water and of ammonium chloride solns. by means of lampblack.......... 940
Enzymes, action on starches of diff origin, 1123; influence of aspartic acid and asparagine on hydrolysis of starch by.......... 1866
Equilibrium, electromagnetic hypothesis of the kinetics of heterogeneous, 970; spectrophotometric method for measuring the, and affinity consts. of the phenolphthaleins and phenolsulfonephthaleins.......... 1031
Esters, ketonic, 422; prepn and hydrolysis of, derived from the substituted aliphatic alcs., 424; addition of nitromethane to unsatd.......... 764
Ethers, cyclic, from *o*-allyl phenols, 648, certain amino and acylamino phenol.......... 1450
o-Ethoxy-benzylphenylurea, and hydrochloride.......... 386, 387
Ethyl alcohol, oxidation by means of $KMnO_4$.......... 1267
Ethylene, analysis of mixts. of, and acetylene.......... 1180
Ethylene chloride, action of Na_2S on.......... 1430
Ethylenechlorohydrin, 1414, coumarane from phenol and.......... 669
Ethyl ether, relations between distribution ratio, temp. and concn. in system: water–succinic acid–, 1501, 721; equation of state for liquids and vapors—vapor phase of, 589; system: water succinic acid–.......... 1719
Ethylhydrocupreidine, and derivs.......... 830, 831
Ethylhydrocupreine, derivs. of, 824, 825; quaternary salts of.......... 2118
Ethyl iodide, prepn. of.......... 797
2-Ethylmercapto-6-chloro-4-aldehydopyrimidine, and derivs.......... 813, 814
2-Ethylmercapto-6-oxy-4-aldehydopyrimidine, diethylacetal of, and action of P halides on.......... 813
1-Ethyl-6-phenyl-2,4-diketohexahydrocyanidine.......... 387
Explosives, Chimica delle sostanze esplosive (Giua, book review).......... 1878

FATS, Edible (Mitchell, book review).......... 476
Fatty acids, volatility with steam of lower, in dil. aq. solns.......... 1946
Feces, estn of S in.......... 1494
Feeding stuffs, estn. of S in.......... 1494
Ferric arsenate, etc. See *Iron arsenate*, etc.
Ferrocyanides, detn of.......... 1776
Fibrin, swelling of, in alkalies.......... 1503
Fibroin, destructive distn. of.......... 1147
Film, measurement of the thickness of, formed on glass and sand.......... 477
Flavone, synthesis of, derivs.......... 83
Flavone-azo-*β*-naphthol, synthesis of, dyes.......... 83
Flavonols, 1285, reduction with Mg and some org. acids.......... 215
Fluorine, crit. study of the K and Na double salts of PbFl as sources of.......... 1477
Foods, Chemistry of (Sherman, book review), 847; detn. of S in.......... 1317, 1494
Formic acid, cond. of alk earth formates in anhydrous, 72; behavior of mixts. of 2 salts contg. a common ion in anhydrous, soln, 1921, transference numbers of the formates of Na, K and Ca in anhydrous, 1934; volatility with steam in dil. aq. soln.......... 1946
Formulas, modified graphic, for org cyclic compds.......... 1029
French, Chem (Dolt, book review).......... 474
Fructose, mutarotation of.......... 559

GALLIUM, purification by electrolysis, and the compressibility and d. of, 133; extn. from Zn oxide, 947; sepn. and detn. of, when assocd with Zn.......... 1491
Gallium chloride, purification by sublimation and analysis of.......... 131
Galvanometer.......... 1362
Gas, automatic variation of, pressure and its application to circulation of.......... 53
Gelatin, mutarotation of, and its significance in gelation.......... 135
Gelation, mutarotation of gelatin and its significance in.......... 135
Gels. See *Colloids*
Gentian violet, its selective bactericidal action.......... 2083
Germanium, extn. from Zn oxide.......... 947
Glass, permanent marking of, vessels, 359; measurement of the thickness of film formed on.......... 477
Glucophores.......... 857
Glucose, mutarotation of.......... 559
Glycol, oxidation of.......... 1385
Glycollic aldehyde, oxidation of.......... 1385
Glycollic acid, oxidation of.......... 1385
Glycyl-arsanilic acids, N-substituted.......... 1909

Glyoxal, oxidation of 1385
Glyoxalic acid, oxidation of 1385
Gold, detn. of, especially in animal tissue 1
Grignard reagent, action of halogens on the 287

HALOGENATION, 287, 292, 1312; of juglone, 833; replacement of sulfonic groups by Cl and the prepn. of org. chloro-derivs. 2028
Halogen-oxy acids, zirconyl compds with the 1722
Halogens, action on the Grignard reagent and the replacement of halogen atoms by one another, 287; liquid NH_3-Na method for, in org. compds., 1051; detn. of the 1898
Helvetica Chimica Acta (book review) 1150
Hexanitro-diphenylamine, prepn. from chlorobenzene 1013
History, of four-membered cyclic ureas, 370, of Scientific Developments (Sarkar, book review), 475; of Chemistry (Moore, book review), 853; Chemistry in Old Philadelphia (Smith, book review) 1313, 1704
Homo-antiarol 806
p-Homosalicylaldehyde, derivs. of 268
Hydrazine, action of Cl on 124
Hydrocarbons, influence of catalysts on the chlorination of, 120, dielec. consts. of typical aliphatic and aromatic 2002
Hydrochloric acid, applicability of the pptd Ag-AgCl electrode to the measurement of the activity of, in extremely dil solns, 1175; free energy of formation of gaseous 1991
Hydrocinchonidine, hydrochloride 820
Hydrocinchonine, hydrochloride 826
Hydrocupreidine, and derivs, 827, 828, 829; azo dyes derived from 2131
Hydrocupreine, and derivs., 821, 823; quaternary salts of, 2117; azo dyes derived from 2131
Hydrogen, overvoltage, 194, chem. action produced by Ra emanation—combination of O and, 531; normal, *vs.* the normal calomel electrode, 1090; reduction of dihydroxy-thymoquinone by means of Pd-, 1873; occlusion by metal electrodes, 1887, 1892, 1895, 1897; overvoltage —applications of its variation with pressure to reduction, metal soln. and deposition 2013
Hydrogen chloride. See *Hydrochloric acid*
Hydrogen halides, vapor pressure and free energies of the, in aq. soln 1991
Hydrogen ion, influence of, concn. on enzymic activity of 3 typical amylases, 231; contrasting effects of chlorides and sulfates on the, concn. of acid solns. 1981
Hydrolysis, of esters derived from the substituted aliphatic alcs 424
Hydronitrogens behavior of the, and their derivs in liquid NH_3 1769
Hydroquinidine, hydrochloride, 826; quaternary salts of 2115
Hydroquinine, and hydrochloride, 819, 820; quaternary salts of 2101
α-Hydroxy acids, rotatory powers of the amides of several, of the sugar group 1141
2-Hydroxy-3-allylbenzoic acid, and dibromide 665
2-Hydroxy-3-allylmethylbenzoate, and dibromide 664
Hydroxyanthraquinones, certain metallic derivs of 2081
8-Hydroxy-2,3-dibromojuglone 840
Hydroxy-ethylphenyl ether, coumarane from 669
2′-Hydroxyflavone 95, 97
3′-Hydroxyflavone 96, 98
4′-Hydroxyflavone 96, 98
Hydroxylamine, action of Cl on, 124; volumetric detn. of 1363
Hydroxymethyl-anthraquinones, analysis of *Rumex crispus*, and a comparison of its, with those from certain other drugs 693
p-Hydroxyphenyl-arsonic acid, prepn. of Na salt of 431
Hydroxyphenyl-arsonic acids, isomeric 1440
β-*p*-Hydroxyphenyl-hydrocinnamic acid 101
γ-Hydroxypropyl phenyl ether, and chromane therefrom 668

ILEX vomitoria, as a native source of caffeine 1307
Indicators, quinone-phenolate theory of, 1031, 1190
Iodimetry, As_2O_3 as a standard substance in 351
Iodine, direct iodinization by means of HNO_3 and, 292; standard, solns 357
Iodinization, direct, by means of I and HNO_3 292
Iodoacetyl-anthranilic acid, ethyl ester of 470
3-Iodobenzoic acid, prepn. of 294
p-Iodocinnamic acid, prepn. of 295
p-Iodonitrobenzene 2047
p-Iodophenylacetic acid, prepn. of 295

4-Iodo-*o*-phthalic acid prepn of 294
β-Iodopropionic acid, isoamyl ester 844
β-Iodopropiophenone 846
Ionization electrolytic, degree of of very dil electrolytes 1951
Ionization, gaseous ratio of chem action to 546
Ions electrolytic activities of of strong electrolytes 1086 1378 intermediate and complex—soly product and activity of the ions in bi-bivalent salts 1155 behavior of mixts of 2 salts contg a common in anhydrous formic acid soln 1921
Iron Chem Analysis of (Blair book review) 1315, electrometric titrations with special reference to the detn of ferrous and ferric 1337 HCl color method for detg 1531
Iron alizarate 2082
Iron arsenate influence of the age of on its peptization 713
Isoamyl iodide prepn of 798
Isocyanic acid, condensation with a Schiff base 379
Isomorphism 1543
Isosterism 1543

JACK bean translocation of the mineral constituents of the 282
Jellies by slow neutralization 763
Juglone halogenation of 833

KETONES 411
δ-Ketonic acid reduction of 1135
Ketonic esters bromination and bromine derivs of certain 683
Kinetics electromagnetic hypothesis of the of heterogeneous equil 970

δ-LACTONE bromination of unsatd 688
Lamp black emulsification of water and of NH_4Cl solns by means of 940
Laws of concn ' solns general b p law 729
Lead potassium fluoride as source of F 1477
Lead sodium fluoride as source of F 1477
Lead tetrafluoride K and Na double salts of as sources of F 1477
Lecithin and Allied Substances (Maclean book review) 853
Lipins (*Maclean* book review) 853 1230
Liquids equation of state for 589 unique case of a that exhibits a min soly in an unstable region 741, structure of 970

MAGNESIUM *m* bromotoluene action of I on 290
Magnesium *o*-bromotoluene action of I on 290
Magnesium *p* bromotoluene action of I on 290
Magnesium *p* bromotoluene action of Cl on 292
Magnesium ethyl bromide action of I on 290
Magnesium ethyl iodide action of bromine on 291
Magnesium phenyl bromide action of I on 288 action of Br on 291 action of Cl on 291
Magnesium phenyl iodide action of I on 289 action of Br on 291 action of Cl on 292
Magnesium *n*-propyl iodide action of bromine on 291
Manganous potassium tartrate 934
Manganous tartrate 934
Mannite See *Mannitol*
Mannitol, some physical properties of and its aq solns 1707
α-*d*-Mannoheptonic acid, amide of 1140
Meat, supposed occurrence of methylguanidine in 1109
Mercuric acetate oxidation of creatine by 1109
Mercuric thiocyanate, addition compd with quinoline 1028
Mercurous chloride, normal H *vs* the normal, electrode 1090
Mercurous thiocyanate addition compd with quinoline 1028
Mercury vapor pressures of in the range 120° to 250° 1783
Mercury compounds org derived from *p*-bromo dimethylaniline 1841
Metal, occlusion of H and O by electrodes, 1887 1892, 1895, 1897, H overvoltage—applications of its variation with pressure to, soln and deposition 2013
2-Methoxy-4-ethoxyacetanilide 1469
3-Methoxy-4-ethoxyacetanilide 1461
4-Methoxy-5-ethoxyacetanilide 1462
4-Methoxy-6-ethoxyacetanilide 1470
2-Methoxy-4-ethoxyaniline 1470

3-Methoxy-4-ethoxyaniline 1461
4-Methoxy-5-ethoxyaniline 1462
4-Methoxy-6-ethoxyaniline 1470
2-Methoxy-4-ethoxy-chloroacetanilide 1470
3-Methoxy-4-ethoxy-chloroacetanilide 1462
4-Methoxy-5-ethoxy-chloroacetanilide 1463
4-Methoxy-6-ethoxy-chloroacetanilide 1471
N-Methyl-*p*-am-idophenol sulfate, prepn. of 270
5-Methylamino-uracil 788
3-Methylbenzoylene-urea 2062
γ,γ-Methylbenzoyl-β-phenyl-butyrolactone 997
γ,γ-Methylbenzoyl-β-phenyl-butyrolactone-carboxylic acid, Me ester 997
3-Methyl-5-bromo-uracil 787
Methylcapsaicin 1116
2-Methyl-5-chloro-acetylamino-phenol 459
4-Methyl-5-chloro-acetylamino-phenol 459
α-Methylcoumarane 655, 657
Methyl-α,α-dimethyl-β-phenyl-γ-benzoyl butyrate, bromination of 687
Methylene-coumaranes 648
3,4-Methylenedioxy-chloroacetanilide 1457
Methylene-diurethane, and amines 1012
α-Methylene-β-naphtho-dihydrofurane 663
Methylguanidine, supposed occurrence of, in meat 1109
Methyl iodide, prepn. of 796
3-Methyl-4-methoxy-acetanilide 1453
2-Methyl-4-methoxy-aniline 1454
3-Methyl-4-methoxy-aniline 1453
2-Methyl-4-methoxy-chloroacetanilide 1454
3-Methyl-4-methoxy-chloroacetanilide 1454
1-Methyl-5-methylamino-uracil, and picrate 786
3-Methyl-5-methylamino-uracil 788
o-Methyl-α-methylene-coumarane 662
p-Methyl-α-methylene-coumarane 662
3-Methyluracil, prepn. of 786
Metol, prepn. of 270
Milk, forms of N in protein-free 388
Molasses, compn. and calorific value of, derived from sugar cane 1432
Molecular weights, detn. of, by the b.-p. method 738
Molecules, arrangement of electrons in 868
Molybdenum, clean-up of N by a heated, filament 167
Monazite, analysis of 47, 49
Mustard gas. *See β,β'-Dichloroethyl sulfide*
Myricetin 215
Myricitrin 215

NAPHTHALENE, new type of, dyes 833
β-Naphthol, derivs. of 663
α-Naphthylamine, carbonyl-diurethane and 1011
β-Naphthylamine, carbonyl-diurethane and 1010
Neutral salt action, on activity of ptyalin, 228; catalysis 1092
Nickel alizarate 2082
Nitration, of sucrose 235
Nitridation, electrolytic, of various anodes in a soln. of NH_4N_3 1769
Nitric acid, iodinization by means of I and 292
Nitrites, detn. of 524
Nutrition, Chemistry of (Sherman, book review) 847
5-Nitro-2-acetamino-benzoic acid, and salts 2065
5-Nitro-2-aminobenzoic acid, and derivs 2066
m-Nitroaniline-sulfonic acid, action of Cl on 2037
o-Nitroaniline-sulfonic acid, action of Cl on 2036
p-Nitroaniline-sulfonic acid, action of Cl on 2036
m-Nitro-*p*-anisidine 1455
6-Nitro-benzoylene-urea, and Na salt 2058, 2059
Nitro-benzoylene-ureas, synthesis of certain 2052

p-Nitrobenzyl cyanide 2047
p-Nitrobromobenzene 2047
Nitrobromopaeonol, and phenylhydrazone 262, 263
Nitro-γ,γ-bromophenyl-butyrophenone 1382
γ-Nitro-γ-bromo-β-phenylpropyl-(4-bromophenyl) ketone 1647
β-Nitro-γ-bromo-γ-phenylpropyl-tertiarylbutyl ketone 1703
p-Nitrochlorobenzene 2046
Nitrocyclopropane, derivs. of 1379, 1644, 1697
2-Nitroflavanone 104
Nitrogen, clean-up of, by a heated Mo filament, 167; forms of, in protein-free milk, 388; passage of trivalent to pentavalent, 631; combination of asymmetric, with asymmetric C and N atoms, 634; distribution in soft corn, 1212; cause of, and remedy for certain inaccuracies in Hausmann's, distribution method, 1526, genesis of petroleum as revealed by its, constituents 1690
Nitrogen compounds, space representation of org 622
Nitrogen oxides, replacement of sulfonic groups by nitro groups by means of nitrous gases 2039
Nitro groups, replacement of sulfonic groups by 2039
p-Nitro-*o*-iodotoluene 2047
Nitromalonic aldehyde, condensation of amino compds. with, 770; condensation of β-aminopropiophenone with 1020
Nitromethane, addition to unsatd. esters 764
3-Nitro-4-methoxy-chloroacetanilide 1455
6-Nitro-2-methyl-4-quinazolone 2067
5-Nitro-2-nitrouramino-benzoic acid, and Me ester 2063, 2064
Nitropaeonol, and derivs 263
o-Nitrophenol-4-sulfonic acid, action of Cl on 2035
p-Nitrophenol-2-sulfonic acid, action of Cl on 2036
1-Nitro-2-phenyl-3(4-bromobenzoyl)cyclopropane 1649
γ-Nitro-β-phenyl-α-bromopropyl-(4 bromophenyl) ketone 1647
γ-Nitro-β-phenyl-α-bromopropyl-tertiary butyl ketone 1699
β-Nitro-γ,γ-phenyl-chloropropyl-(4-bromophenyl) ketone 1650
γ-Nitro-β-phenyl-α-iodopropyl-(4-bromophenyl) ketone 1648
o-Nitrophenyl-methylene-diurethane 1012
γ-Nitro-β-phenylpropyl-(4-bromophenyl) ketone 1646
γ-Nitro-β-phenylpropyl-tertiary butyl ketone 1699
6-Nitro-4-quinazolone 2067
Nitro-resodiacetophenone, and derivs 266
Nitrotoluenes, oxidation of *o*-, *m*- and *p*- 1561
Nitrous acid, detn. of 524
Nomenclature, of four-membered cyclic-ureas 370

OCCLUSION, of H and O by metal electrodes 1887, 1892, 1895, 1897
sec.-Octylhydrocupreine, dihydrochloride 825
Oils, Edible (Mitchell, book review) 476
Oleic acid, Te salt of 344
Orcinol-disulfonic acid, action of Cl on 2035
Organic Chemistry (Richter, book review), 2148; Introduction to (Stoddard, book review), 1705; for Advanced Students (Cohen, book review) 214
Organic compounds, liquid NH_3-Na method for halogens in, 1051; oxidation with alk. $KMnO_4$ 138
Overvoltage, hydrogen 194, 201
Oxalic acid, Te salt of, 344; detn. of 126
Oxidation, of EtOH by means of $KMnO_4$, 1267; of org. compds. with alk. $KMnO_4$, 1385; side chain, with $KMnO_4$, 1559; electrometric method for the detn. of ferrocyanides depending on a change in, potential 177
Oxygen, chem. action produced by Ra emanation—combination of H and, 531; occlusion by metal electrodes 1887, 1892, 1895, 189

PAEONOL, and derivs 26
Palladium, reduction of dihydroxy-thymoquinone by means of, -H 187
Pancreas, proteolytic activity of pancreatic amylase prepns 185
Paraffins, new reaction of 36
Particles, measuring the size of ultramicroscopic, 312, relation between intensity of Tyndall beam and size of 57
Passivity, of Co 19

Pepsin, chem. changes in the purification of 221
Peptization, influence of the age of ferric arsenate on its 713
Peptone, compressibility of aq. solns. of 346
Perselenates, attempts to prepare 964
Perselenic acid, attempts to prepare 964
Petroleum, genesis of, as revealed by its N constituents 1690
Phenacetyl-(4-bromobenzyl)methane 1655
Phenacetyl-trimethylacetyl methane 1702
Phenacylarsanilic acid, substituted 1826
α-Phenacyl-β,β-chlorophenyl-propionic acid, Et ester 1103
Phenacyl esters 75
α-Phenacyl-β-nitropropionic acid, methyl ester of 769
α-Phenacyl-β′-nitropyrrole 1025
Phenetole, nitro deriv. of 2043
Phenetole-sulfonic acid, action of Cl on 2031
Phenol, interaction of arsenic acid and, 432, chromane from, and trimethylene-chlorohydrine, 669; coumarane from, and ethylene-chlorohydrine, 669; direct arsenation of, 1440; certain amino and acylamino, ethers 1450
Phenolate, quinone-, theory of indicators 1031, 1190
Phenolphthaleins, spectrophotometric method for measuring the equil. and affinity consts. of the 1031
Phenols, alkali-insol 247
Phenolsulfonic acid, action of Cl on 2032
Phenolsulfonephthalein, reactions of, and its bromo and nitro derivs, and their monobasic and dibasic salts 1190
Phenolsulfonephthaleins, spectrophotometric method for measuring the equil. and affinity consts. of the 1031
Phenol-tetrabromophthalein, and some of its derivs 1289
Phenoxyacetyl arsanilic acids, amides of (4-arsonic acid)-phenoxyacetic acid and the isomeric 1834
β-Phenoxy-cinnamic acid 87
Phenoxy-ethylarsanilic acid, substituted 1826
β-Phenoxy-hydrocinnamic acid, and Ba salt of a disulfonic acid of 100, 103
Phenylacetic acid, iodimization of 295
4-Phenyl-5-acetopyrazoline-carboxylic acid, ethyl ester 1108
4-Phenyl-5-acetylpyrazoline-dicarboxylic acid-3,5, ethyl ester 1108
N-(Phenyl-4-arsonic acid)-α-phenylglycine, and its amides 1822
4-Phenyl-5-benzal-acetopyrazoline-carboxylic acid, Et ester 1107
2-Phenyl-3-benzoyl-cyclopropane-carboxylic acid, and ethyl ester 1101
4-Phenyl-5-benzoyl-pyrazoline-carboxylic acid, ethyl ester 1100
β-Phenyl-γ-(4-bromobenzoyl)butyric acid 1096
β-Phenyl-γ-(4-bromobenzoyl)butyrolactone 1097
Phenyl-(4-bromobenzoyl)pyrazole 1099
Phenyl-(4-bromobenzoyl)pyrazole-carboxylic acid 1098
4-Phenyl-5-(4-bromobenzoyl)pyrazolinecarboxylic acid, Et ester 1099
β-Phenyl-γ-bromo-γ-(4-bromobenzoyl)butyric acid, and methyl ester 1096, 1097
2-Phenyl-3-(4-bromophenyl)cyclopropane-carboxylic acid, ethyl ester 1099
1-Phenyl-3-(4-bromophenyl)furane 1651
4-Phenyl-6-(4-bromophenyl)pyrone-1,2 1099
Phenyl-carbethoxy-biuret, and salts 1007
γ,γ-Phenyl-chloroallyl-(4-bromophenyl) ketone 1650
3-Phenyl-cyclopropane-dicarboxylic acid-2,2 1104
Phenyl-diurethane 1009
Phenylene-diamines, prepn. of 436
1,2-(α-Phenyl-α-ethylcarbinyl)-2-phenyl-cyclopropane 1259
β-Phenylglyoxyl-β-phenyl-α,α-dimethyl-propionic acid 692
β-Phenyl-hydrocoumarin 102
β-Phenyl-hydroxylamine 276
Phenyl-isocyanuric acid 1008
2-Phenyl-3,3-methylbenzoyl-cyclopropane-dicarboxylic acid, and dimethyl ester 998, 999
Phenylmethylenediurethane 1012
1-Phenyl-3-methyl-5-pyrazolone, condensation with anhydrides 707
γ-Phenyl-β-nitroalkyl-(4-bromophenyl) ketone 1652
β-Phenyl-γ-nitro-ethylmalonic acid, methyl ester of 766
γ-Phenyl-β-nitropropenyl-(4-bromophenyl) ketone 1653
4-Phenyl-pyrazole-carboxylic acid, ethyl ester ......

1 Phenyl-2-trimethylacetyl 3-nitrocyclopropane 1700
Phenylurea condensation with benzaldehyde 385, 386
Phthalic acid, iodinization of o-, *294*, derivs 1289, 1293
Phthalimide, prepn of K 843
β-Phthalyl propionic acid, and isoamyl ester 844, 845
β-Phthalyl propiophenone 846
Physical Chemistry System *of* (Lewis book review), 1474, Textbook *of* (Lincoln book review) 1475
Physics, New Science of the Fundamental (Strong book review) 851
Pinene, optically active nitrosochloride and synthetical active 361
Pituitaries method of tissue analysis applied to the posterior and anterior lobes of cattle 1225
Pollen, protein ext of ragweed, 670, yellow coloring substances of ragweed 1285
Polymerization, of water 59
Potassium formate transference number in anhydrous formic acid 1934
Potassium hydroxide decompn of $SnCl_2$ by solns 1969
Potassium lead fluoride as source of F 1477
Potassium manganous tartrate 934
Potassium permanganate, oxidation of EtOH by means of 1267 oxidation of org compds with alk , 1385 side *chain oxidations with* 1559
Potassium plumbate prepn and properties of 1478
Potential electric electrometric method for the detn of ferrocyanide depending on a change in oxidation 1776 of zinc and Cd electrodes 1787
Potentiometers 1359 1361
Pressures detn of the compressibility of solids at high 12 automatic variation of gas 53, chem reactions at low 167 soly —relative values of internal and their practical application 1067
Propyl alcohols esters derived from halogen substituted 428
N Propyl iodide, prepn of 797
Proteins, 1147, 1233 ext of ragweed pollen 670 chem nature of the adsorption of acids and alkalies by the mol 1511
Ptyalin *effect of neutral salts on the activity of* 228
Pump vacuum 53
Pyrazolines ketonic 1098 colored condensation products from ketonic 1105
Pyrimidines 782 810
Pyrogallol synthesis of certain substituted ethers 798

QUANTUM theory (Lewis book review) 1474
Quinazolines 2052
Quinicine, hydrochloride 832
Quinidine hydrochloride 819 quaternary salts of 2099
Quinine hydrochloride 819 quaternary salts of 2095
Quinoline new addition compds of with certain inorg salts 1027
Quinone, phenolate theory of indicators 1031, 1190

RADIUM *emanation* chem action *produced by—combination* of H and O, 531 *chem action* produced by—chem effect of recoil atoms 551
Ragweed, protein ext of pollen 670 yellow coloring substances of pollen 1285
Rare earths 718
α-Rays, action on pure O and H 545
γ-Ray, activity of Th D 50
Rays, Röntgen chem analysis by 1168
Reactions, at low pressures, 167 ratio of chem action to ionization, 546, mechanism of chem action and the structure and properties of compds 887
Reagents, org chem .276, 789
Rearrangement mol in the acylation of certain aminophenols .. 2068
Reduction, *of dihydroxy-thymoquinone by means of Pd-H, 1873 H overvoltage—applications* of its variation with pressure to 2013
Resodiacetophenone, derivs of . .. 265
Resorcinol, *derivs of the ethers of, 1465*, nitro deriv of 2043
Rumex crispus, proximate analysis *of*, and a comparison of its hydroxymethyl-anthraquinones with those from certain other drugs . .. 693

SALICYLALDEHYDE, derivs of 267
Salicylic acid, derivs of 664
Salts, effect of neutral, on the activity of ptyalin, 228, spectrophotometric method for measuring the concns. of the quinoidal and lactoidal, 1031, soly product and activity of the ions in

bi-bivalent, 1155, behavior of mixts of 2 contg a common ion in anhydrous formic acid soln . . 1921
Salvarsan See *Arsphenamine*
Sand, measurement of the thickness of film formed on 477
Saponin, alfalfa 640
Schiff bases, condensation of isocyanic acid with a 379, action of basic reagents on 1862
Science, Hindu Achievements in Exact (Sarkar book review) 475
Selenic acid 949
Selenious acid prepn of 951, electrolytic oxidation to selenic acid 957 detection of, present in selenic acid 961
Selenium, extn from smelter flue dust and from anode slime 950
Selenium dioxide, prepn of 951
Semicarbazide, relations between the chem structures of carbonyl derivs and their reactivities toward salts of 393
Silicic acid, vibration and syneresis of gels 1329
Silver applicability of the pptd AgCl electrode to the measurement of the activity of HCl in extremely dil solns 1175
Silver chloride applicability of the pptd Ag AgCl electrode to the measurement of the activity of HCl in extremey dil solns 1175
Silver selenite oxidation by Br 954
Silver thiocyanate addition compd with quinoline 1028
Sirups, compn and calorific value of derived from sugar cane 1432
Smokes, relation between the intensity of Tyndall beam and concn of 300 disappearance of in a confined space 304 particles in 576 elec precipitator for analyzing 587
Sodium formate transference number in anhydrous formic acid 1934
Sodium lead fluoride, as source of F 1477
Sodium plumbate prepn and properties of 1478
Soil compn of the ash of crab grass as affected by the in which it is grown 1384
Solids, detn of the compressibility of at high pressures 12
Solubility unique case of a liquid that exhibits a min in an unstable region 741 and electromagnetic environment 971 relative values of internal pressures and their practical application, 1067 product and activity of the ions in bi bivalent salts 1155
Solutions compressibility of aq especially of urethane 59 detn of b ps of 721 laws of concd —b p law, 729, measurement of the cond of 1727
Standard solutions arsenious oxide as a standard substance in iodimetry 351
Stannous chloride See *Tin chloride*
Starch, detn of sol in the presence of starch and its hydrolytic cleavage products 107, prepn of sol 113 action of enzymes on of diff origin 1125 influence of aspartic acid and asparagine on the enzymic hydrolysis of 1866
Stirrer, magnetic 53
Succinic acid relations between distribution ratio temp and concn in system water-ether-, 150, Te salt of, 344 system water-ether 1719 relations between distribution ratio, temp and concn in system water-ether 1721
Sucrose, nitration of 235
Sucrose octanitrate 235
Sugar cane, compn and calorific value of sirups and molasses derived from 1432
Sugar group, rotatory powers of the amides of several α-hydroxy acids of the 1141
Sugars, retardation by of diffusion of acids in gels 358
Sulfates, estn of, in a concd electrolyte 1317 contrasting effects of chlorides and, on the H ion concn of acid solns 1981
o-Sulfobenzoic acid, prepn of the acid NH_4 salt and anhydride of 1197
3-Sulfo-*p*-hydroxybenzoic acid action of Cl on 2038
Sulfonic groups, replacement by Cl 2028 replacement by nitro groups 2039
***p*-Sulfophenylazo-*m*'-ethoxyphenol** 1467
***p*-Sulfophenylazo-*o*'-ethoxyphenol** 1458
***p*-Sulfophenylazo-guaiacol** 466
***p*-Sulfophenylazo-*m* methoxyphenol** 1465
Sulfosalicylic acid, action of Cl on 2037
Sulfur, standardization of the, b p, 745, detn in foods, 1317 estn in feeds, feces and foods 1494
Sulfur dioxide, thermal dissoc of .. 69
Sulfuric acid, detection in the presence of selenic acid . 963
Surface energy, effects of acids and bases on the, relations of β,β'-dichloroethyl-sulfide 1977
Surface tension, detn of, and the wt of falling drops—surface tension of water and benzene by the capillary height method, 499, formulas concerning 620

Suspensions, relation between the intensity of Tyndall beam and concn. of 300
Swelling, of fibrin in alkalies 1503
Syneresis, of silicic acid gels 1329
Syringic acid, new acetophenetide derived from the ethyl ether of 798
Systems, relations between various functions of the variables of ternary 1718

TALCUM, use of coal as a substitute for, to induce rapid boiling 1189
Tanning, chrome 1981
Tartaric acid, Te acid salt of 342
Tartrates, test for, depending on the formation of the Cu-tartrate complex 207
Taste, new theory relating constitution to 855, 1378
Tellurium salts, prepn. of certain org 342
Tellurium sulfide, chemistry of 329
Temperature, standardization of the S b. p., 745; Methods of Measuring (Griffiths, book review), 850; calcn. of the, coeff. of the distribution ratio, 1718; relations between distribution ratio, and concn. in system: water–ether–succinic acid 150, 1721
Terpenes, synthesis of some homologs of the 1676
Tetrabromoeosin, and derivs 1293
Tetrabromofluoran 1291
Tetrabromofluorescein, and derivs 1293
Tetrabromofluorescein-carbinol-carboxylic acid, and di-NH_4 salt 1295
Tetrabromo-phenolsulfonephthalein, and di-NH_4 salt 1205, 1206
Tetrabromo-phenoltetrabromo-phthalein, and derivs 1292
Δ'-Tetrahydroterephthalic acid, hydrocarbons from 1684
Tetranitro-diphenylamine 1017
Tetranitromethane, vapor pressure of 1336
Tetranitro-phenolsulfonephthalein, and di-NH_4 salt 1206, 1207
Tetraphenyldiarsine 2048
Thallium alloys, concd 1732
Thiodiglycol 1427
Thioglycollic acid, some metallic derivs. of ethyl ester of 777
Thorium, emanation method of detg 42
Thorium D, gamma ray activity of 50
Thymol, action of 10%, -$CHCl_3$ preservative on the Cl content of urine, 440; nitro deriv. of 2042
Thymolsulfonic acids, action of Cl on 2034
Tin chloride, decompn of $SnCl_2$ by water and by KOH solns 1969
Tissue, animal, detn. of Au in, 1; method of analysis—applied to the posterior and anterior lobes of cattle pituitaries 1225
Titration, electrometric, with special reference to the detn. of *ferrous and ferric Fe, 1337*; elec. app. for use in electrometric 1358
o-Tolylallophanic acid, ethyl ester 1010
o-Tolylisocyanuric acid, and Ag salt 1009
Transference numbers, of the formates of Na, K and Ca in anhydrous formic acid 1934
ω-Tribromo-bromopaeonol 262
2,3,8-Tribromojuglone, and Na salt 838, 839
2,4,6-Trichloro-3-acetaminophenol 463
N,N'-β,β,β-Trichloro-ethylidene-bis-*m*-nitraniline 1864
N,N'-β,β,β-Trichloro-ethylidene-bis-*o*-nitraniline 1863
N,N'-β,β,β-Trichloro-ethylidene-bis-*p*-nitraniline 1864
Trichloromethyl group, action of CuCl with compds. contg. the 1129
Trimethylene-chlorohydrine, chromane from phenol and 669
2,4,6-Trinitro-*m*-cresol 2046
2,4,6-Trinitrophenol 2044, 2045
2,4,6-Trinitroresorcinol 2044, 2045
1,1,4-Triphenyl-2-benzoyl-4-chlorobutene-3 1260
α,γ,ε-Triphenyl-*β*-bromo-pentanedione-*α,ε* 1253
α,γ,ε-Triphenyl-*β,δ*-dibromo-pentanedione-*α,ε* 1253
Triphenylmethyl 1655
Trisulfo-*m*-hydroxybenzoic acid, action of Cl on 2037
Tyndall beam, relation between the intensity of, and concn. of suspensions and smokes, 300; relation between intensity of, and size of particles 575
Tyndallmeter 297

ULTRAMICROSCOPE 315
Ultramicroscopic particles, measuring the size of 312

o-Uraminobenzoic acid, and Me ester ... 2055, 2056
Urea, action of Cl on ... 124
Ureas, four-membered cyclic, 370, 379; action of NH$_3$ and amines on the substituted ... 1004
Ureides, and β-substituted ureides of *N*-arylglycine-arsonic acids ... 1600
Urethan, compressibility of aq. solns., 59; action of NH$_3$ and amines on the substituted derivs. of ... 1004
Urine, action of 10% thymol-CHCl$_3$ preservative on the Cl content of ... 440

VALENCE, coördination number and covalence, 926; relation of the intensity of the intermol. electromagnetic field to cohesion and ... 974
Vanillyl acyl amides ... 2121
Vanillylamine, synthesis of ... 1118
Vapor pressures, of the H halides in aq soln ... 1991
Vapors, equation of state for ... 589
Vegetable material, detn. of caffeine in ... 1298
***Vibration*, of silicic acid gels** ... 1329
"Vuzin" ... 825

WATER, polymerization of, 59; relations between distribution ratio, temp and concn. in system: ether–succinic acid–, 150, 1721; surface tension of, 499; emulsification of, and of NH$_4$Cl solns. by means of lampblack, 940; adsorption of the interface, -benzene as compared with that on the surface of the water, 990; system: Et$_2$O–succinic acid–, 1719; decompn. of SnCl$_2$ by ... 1969
Weighing, single deflection method of ... 1151
Woodhouse, James (Smith, book review) ... 710

1,2,4-XYLENOL, nitro deriv. of ... 2042
1,3,4-Xylenol, nitro deriv. of ... 2042
1,4,5-Xylenol, nitro deriv. of ... 2042
Xylose, prepn. from corn cobs ... 1002

YTTRIUM, at wt. of ... 718

ZINC, detn. as the sulfide, 487, 992; sepn. and detn of Ga when assocd. with, 1491; potential of the, electrode ... 1787
Zinc acetate, addition compd with quinoline ... 1028
Zinc oxide, extn. of Ga and Ge from ... 947
Zirconium, detn. of ... 1801
Zirconium phosphate, precipitation of ... 1802
Zirconyl chlorate ... 1725
Zirconyl compounds, with the oxy-halogen acids ... 1722
Zirconyl iodate ... 1722
Zirconyl perchlorate ... 1724